NMCP COVID-19 Literature Report #75: Friday, 27 August 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

"The U.S. is projected to see nearly 100,000 more COVID-19 deaths between now and Dec. 1, according to the nation's most closely watched forecasting model" (AP).

"The coronavirus is here forever. This is how we live with it. We can't avoid the virus for the rest of our lives, but we can minimize its impact" (Atlantic).

"Would it be fair to treat vaccinated Covid patients first? Last week, Texas health care policymakers discussed taking vaccination status into account for Covid triage. It's a larger conversation ethicists are bracing for" (Wired).

Around the World

"Iceland has been a vaccination success. Why is it seeing a coronavirus surge?" (WP).

"Ultra-vaxxed Israel's crisis is a dire warning to America" (Daily Beast).

New Zealand has extended its national lockdown after 70 new cases were reported (Guardian).

Data

The CDC announced it is standing up "a new center designed to advance the use of forecasting and outbreak analytics in public health decision making" (CDC).

"How CDC data problems put the U.S. behind on the delta variant" (WP).

Long read: "Inside America's Covid-reporting breakdown – Crashing computers, three-week delays tracking infections, lab results delivered by snail mail: State officials detail a vast failure to identify hotspots quickly enough to prevent outbreaks" (Politico).

Pandemic Preparedness

"Has COVID taught us anything about pandemic preparedness? – Researchers warn that plans to prevent the next global outbreak don't consider the failures that have fuelled our current predicament" (Nature).

"New report calls for preventing human pandemics at the animal source" (Axios; see also: full report from Harvard Global Health Initiative).

"US health security at risk because of medicine manufacturing limits" (WUSTL).

Commentary: "The Pentagon must prep now for the next pandemic – We must take stock of the myriad ways the U.S. military has helped fight COVID-19—and learn to do even better" (Defense One).

Upcoming Events

TOPIC: The Fourth Wave — Vaccines, Variants, and the Future
– APHA/NAM webinar series

WHEN: Wednesday 01 September 2021, 1700-1830 EDT

DETAILS: "The latest COVID-19 Conversations webinar will provide an update on the current state of COVID-19, focusing specifically on the delta variant, implications for children under the age of 12, what the rise of this highly infectious variant means for vaccinated and unvaccinated adults and adolescents, and what it will take to move past this surge and end the pandemic."

REGISTER: https://covid19conversations.org/Webinar-Registration

TOPIC: Towards a Post-Pandemic World: Lessons from COVID-19 for Now and the Future
– The National Academies of Sciences, Engineering, and Medicine (NASEM)
– Free virtual workshop

WHEN: 21-24 September 2021, 1000-1430 EDT

DETAILS: "Join the Forum on Microbial Threats for an exciting virtual conversation about what we've learned from 15 months of living through a global pandemic. The workshop will broadly examine responses to COVID-19 in the U.S. and abroad, and will host retrospective and prospective discussions on the broad impacts of the pandemic on human health and society. Events will highlight successes, missed opportunities, and emerging data in order to extract key understandings that leaders in governments, public health systems, the private sector, and communities can incorporate into their ongoing pandemic responses now with a view towards enhancing resilience and preparedness for future outbreaks.

Individual workshop sessions will focus on:

- Anticipated long-term effects of COVID-19 (Day 1)
- Trust, engagement, and misinformation in public health (Day 2)
- Key questions on interventions and recovery from COVID-19 (Day 3)
- Building capacities for better pandemic preparedness and response (Day 4)"

For the agenda and more information, see: https://www.nationalacademies.org/event/07-27-2021/moving-past-covid-19-lessons-learned-from-responses-around-the-world

Register at: https://www.eventbrite.com/e/towards-a-post-pandemic-world-lessons-from-covid-19-for-now-and-the-future-tickets-159698413253

Journal Articles

Sci Adv: Excess of COVID-19 cases and deaths due to fine particulate matter exposure during the 2020 wildfires in the United States (13 August 2021)

> "The year 2020 brought unimaginable challenges in public health, with the confluence of the COVID-19 pandemic and wildfires across the western United States. Wildfires produce high levels of fine particulate matter ($PM_{2.5}$). Recent studies reported that short-term exposure to $PM_{2.5}$ is associated with increased risk of COVID-19 cases and deaths. We acquired and linked publicly available daily data on $PM_{2.5}$, the number of COVID-19 cases and deaths, and other confounders for 92 western U.S. counties that were affected by the 2020 wildfires. We estimated the association between short-term exposure to $PM_{2.5}$ during the wildfires and the epidemiological dynamics of COVID-19 cases and deaths. We adjusted for several time-varying confounding factors (e.g., weather, seasonality, long-term trends, mobility, and population size). We found strong evidence that wildfires amplified the effect of short-term exposure to $PM_{2.5}$ on COVID-19 cases and deaths, although with substantial heterogeneity across counties."

SARS-CoV-2 Virus and Variants

News in Brief

"Delta's rise is fuelled by rampant spread from people who feel fine – People infected with the Delta variant generally do not have COVID-19 symptoms until two days after they start shedding the coronavirus" (Nature).

"The mutation that helps Delta spread like wildfire – A key amino-acid change might underlie the coronavirus variant's ferocious infectivity" (Nature).

Long Reads – Viral Evolution

"The coronavirus could get worse – Delta is far from the last variant. But what shape the virus takes next depends on us" (Atlantic).

"Viral evolution 101: Why the coronavirus has changed as it has, and what it means going forward" (STAT).

"Evolving Threat – New SARS-CoV-2 variants have changed the pandemic. What will the virus do next?" (Science).

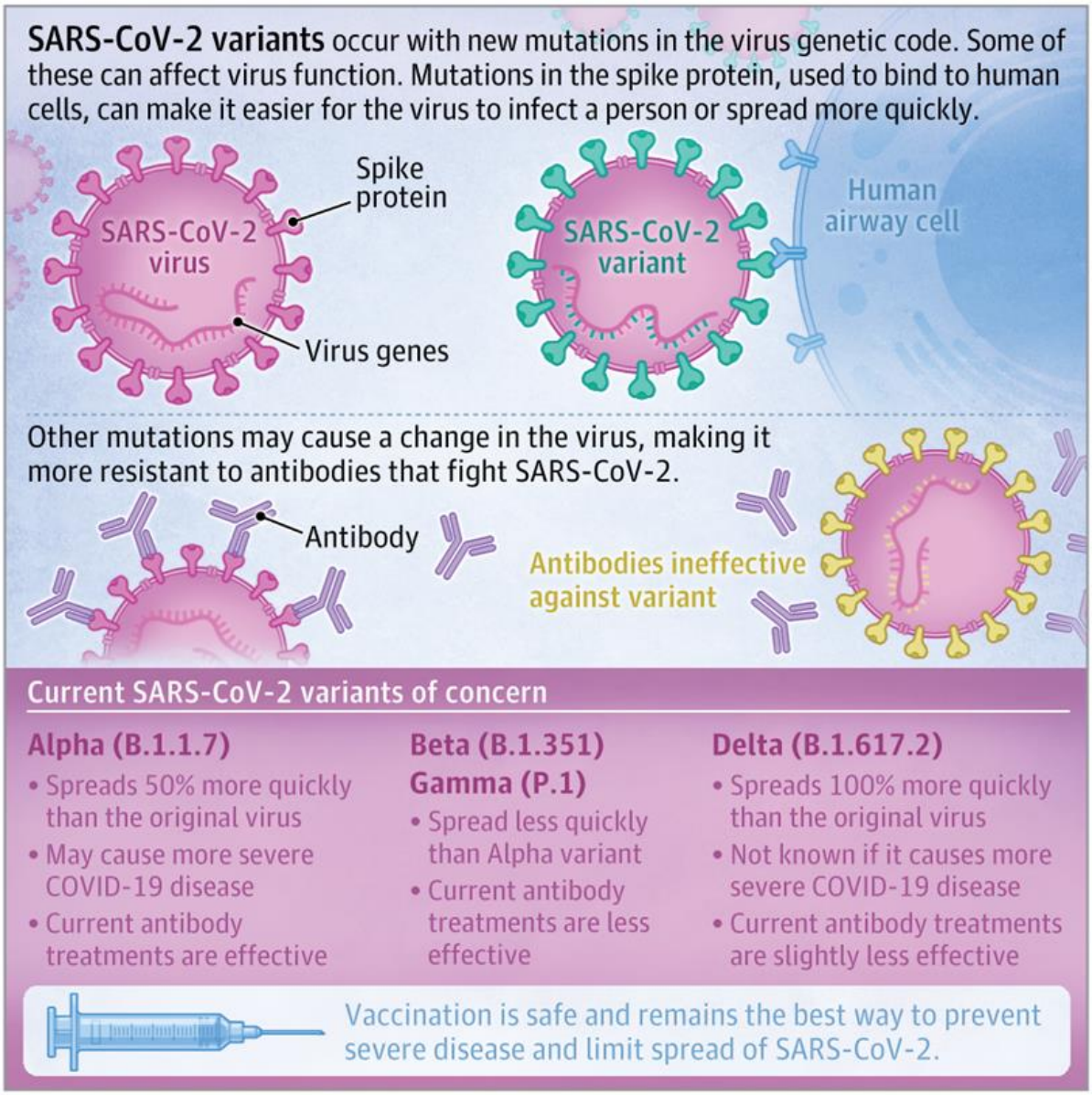
Long Reads – Virus Origins

"How COVID-19's origins were obscured, by the East and the West" (BAS).

"Origins of SARS-CoV-2: window is closing for key scientific studies – Authors of the March WHO report into how COVID-19 emerged warn that further delay makes crucial inquiry biologically difficult" (Nature).

Special Reports and Other Resources

This JAMA Patient Page "Variants of SARS-CoV-2" graphic offers a good cheat sheet on the variants; see also: CDC's "SARS-CoV-2 Variant Classifications and Definitions" website. (Image shared without permission.)



Journal Articles

Clin Infect Dis: Clinical and virological features of SARS-CoV-2 variants of concern: a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.315 (Beta), and B.1.617.2 (Delta) (23 August 2021)

> "Background: The impact of SARS-CoV-2 variants of concern (VOCs) on disease severity is unclear. In this retrospective study, we compared outcomes of patients infected with B.1.1.7, B.1.351, and B.1.617.2 with those with wild-type strains from early 2020.
>
> Methods: National surveillance data from 1-January-2021 to 22-May-2021 were obtained from the Ministry of Health, and outcomes in relation to VOC were explored. Detailed patient level data from all patients with VOC infection admitted to our center between 20-December-2020 and 12-May-2021 were analyzed. Clinical outcomes were compared with a cohort of 846 patients admitted from January-April 2020.
>
> Results: 829 patients in Singapore in the study period were infected with these 3 VOCs. After adjusting for age and sex, B.1.617.2 was associated with higher odds of oxygen requirement, ICU admission, or death (adjusted odds ratio (aOR) 4.90, [95% CI 1.43-30.78]). 157 of these patients were admitted to our center. After adjusting for age, sex, comorbidities, and vaccination, aOR for pneumonia with B.1.617.2 was 1.88 [95% CI 0.95-3.76]) compared with wild-type. These differences were not seen with B.1.1.7 and B.1.351. Vaccination status was associated with decreased severity. B.1.617.2 was associated with significantly lower PCR Ct values and longer duration of Ct value ≤30 (median duration 18 days for B.1.617.2, 13 days for wild-type).
>
> Conclusions: There was a signal toward increased severity associated with B.1.617.2. The association of B.1.617.2 with lower Ct value and longer viral shedding provides a potential mechanism for increased transmissibility. These findings provide an impetus for the rapid implementation of vaccination programs."

NEJM: Pan-Sarbecovirus Neutralizing Antibodies in BNT162b2-Immunized SARS-CoV-1 Survivors (18 August 2021)

> "Emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern pose a challenge to the effectiveness of current vaccines. A vaccine that could prevent infection caused by known and future variants of concern as well as infection with pre-emergent sarbecoviruses (i.e., those with potential to cause disease in humans in the future) would be ideal. Here we provide data showing that potent cross-clade pan-sarbecovirus neutralizing antibodies are induced in survivors of severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) infection who have been immunized with the BNT162b2 messenger RNA (mRNA) vaccine [Pfizer–BioNTech]. The antibodies are high-level and broad-spectrum, capable of neutralizing not only known variants of concern but also

sarbecoviruses that have been identified in bats and pangolins and that have the potential to cause human infection. These findings show the feasibility of a pan-sarbecovirus vaccine strategy."

Cell: The Origins of SARS-CoV-2: A Critical Review (18 August 2021)

"Since the first reports of a novel SARS-like coronavirus in December 2019 in Wuhan, China, there has been intense interest in understanding how SARS-CoV-2 emerged in the human population. Recent debate has coalesced around two competing ideas: a "laboratory escape" scenario and zoonotic emergence. Here, we critically review the current scientific evidence that may help clarify the origin of SARS-CoV-2."

Emerg Infect Dis: Rapid Increase in SARS-CoV-2 P.1 Lineage Leading to Codominance with B.1.1.7 Lineage, British Columbia, Canada, January–April 2021 (13 August 2021)

"Several severe acute respiratory syndrome coronavirus 2 variants of concern (VoCs) emerged in late 2020; lineage B.1.1.7 initially dominated globally. However, lineages B.1.351 and P.1 represent potentially greater risk for transmission and immune escape. In British Columbia, Canada, B.1.1.7 and B.1.351 were first identified in December 2020 and P.1 in February 2021. We combined quantitative PCR and whole-genome sequencing to assess relative contribution of VoCs in nearly 67,000 infections during the first 16 weeks of 2021 in British Columbia. B.1.1.7 accounted for <10% of screened or sequenced specimens early on, increasing to >50% by week 8. P.1 accounted for <10% until week 10, increased rapidly to peak at week 12, and by week 13 codominated within 10% of rates of B.1.1.7. B.1.351 was a minority throughout. This rapid expansion of P.1 but suppression of B.1.351 expands our understanding of population-level VoC patterns and might provide clues to fitness determinants for emerging VoCs."

Science: Durability of mRNA-1273 vaccine–induced antibodies against SARS-CoV-2 variants (12 August 2021)

"SARS-CoV-2 mutations may diminish vaccine-induced protective immune responses, particularly as antibody titers wane over time. Here, we assess the impact of SARS-CoV-2 variants B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.429 (Epsilon), B.1.526 (Iota), and B.1.617.2 (Delta) on binding, neutralizing, and ACE2-competing antibodies elicited by the vaccine mRNA-1273 over seven months. Cross-reactive neutralizing responses were rare after a single dose. At the peak of response to the second vaccine dose, all individuals had responses to all variants. Binding and functional antibodies against variants persisted in most subjects, albeit at low levels, for 6-months after the primary series of the mRNA-1273 vaccine. Across all assays, B.1.351 had the lowest antibody recognition. These data complement ongoing studies to inform the potential need for additional boost vaccinations."

Testing

MMWR: Use of Rapid Antigen Testing for SARS-CoV-2 in Remote Communities — Yukon-Kuskokwim Delta Region, Alaska, September 15, 2020–March 1, 2021 (20 August 2021)

> "What is already known about this topic? Until the widespread availability of rapid point-of-care COVID-19 testing, one of the primary challenges in rural Alaska was slow turnaround times for SARS-CoV-2 laboratory-based nucleic acid amplification test results.
>
> What is added by this report? Introduction of rapid, point-of-care antigen testing in Alaska's remote Yukon-Kuskokwim Delta region was followed by a more than threefold reduction in daily SARS-CoV-2 case rates during approximately 1 month before the introduction of COVID-19 vaccination.
>
> What are the implications for public health practice? Rapid point-of-care antigen testing shortens the turn-around time and might be a valuable tool in reducing transmission of SARS-CoV-2 in rural communities by facilitating rapid isolation and quarantine."

JAMA: Change in Saliva RT-PCR Sensitivity Over the Course of SARS-CoV-2 Infection (13 August 2021)

> Research letter: "This study investigates the timeframe that optimizes saliva sensitivity for SARS-CoV-2 detection using reverse transcriptase–polymerase chain reaction (RT-PCR) testing….
>
> Saliva was sensitive for detecting SARS-CoV-2 in symptomatic individuals during initial weeks of infection, but sensitivity in asymptomatic SARS-CoV-2 carriers was less than 60% at all time points. As COVID-19 testing strategies in workplaces, schools, and other shared spaces are optimized, low saliva sensitivity in asymptomatic infections must be considered. This study suggests saliva-based RT-PCR should not be used for asymptomatic COVID-19 screening."

COVID-19 Vaccines

News in Brief

The big news: The Pfizer-BioNTech COVID-19 vaccine was granted full FDA approval on Monday, 23 August 2021; it is the first vaccine approved for the prevention of COVID-19 disease in people over 16 years old (FDA).

Marketed as Comirnaty (koe-mir'-na-tee), '[t]he name is coined from Covid-19 immunity, and then embeds the mRNA in the middle, which is the platform technology, and as a whole the name is meant to evoke the word community'" (Fierce Pharma).

Pfizer has also submitted data to the FDA to gain approval for booster dose (Pfizer).

Moderna's COVID-19 vaccine is expected to be the next one granted full approval (application submitted); according to the European Medicines Agency, it will be called Spikevax (EMA).

Effectiveness

"COVID vaccines protect against Delta, but their effectiveness wanes – Massive UK study of COVID-19 cases shows that people who are jabbed have good immunity at first, but quickly become more vulnerable to the fast-spreading Delta variant" (Nature; see also: preprint [pdf]).

"New evidence points to antibodies as a reliable indicator of vaccine protection" (NPR; see also: medRxiv preprint).

"Scientists unlock clues to determining how safe vaccinated people are from Covid-19" (STAT).

Boosters

"The fine print: Understanding the new policy authorizing extra Covid vaccine doses for the immunocompromised" (STAT).

"U.S. officials' decision on Covid-19 booster shots baffles — and upsets — some scientists" (STAT).

"Do I need a booster if I got the Johnson & Johnson vaccine? Probably at some point, but health officials still are collecting the data needed to decide" (AP).

Speaking of: Johnson & Johnson reported interim data that a booster for its single-shot vaccine "generated a rapid and robust increase in spike-binding antibodies, nine-fold higher than 28 days after the primary single-dose vaccination" (J&J).

"WHO calls for a delay in booster shots to prioritize under-vaccinated countries" (NPR).

Podcast: "Coronapod: COVID boosters amidst global vaccine inequity" (Nature).

Adverse Effects

"U.S. officials reviewing possibility Moderna vaccine is linked to higher risk of uncommon side effect than previously thought" (WP).

"COVID vaccines show no signs of harming fertility or sexual function –The novel coronavirus, in contrast, can disrupt both things in unvaccinated men and women" (Sci Am).

"COVID vaccines and blood clots: what researchers know so far" (Nature).

"Vaccine effect or functional neurological disorder? – COVID vaccination may trigger FND, much like other stressors" (Medpage; see also: J Neurol Neurosurg Psychiatry letter and J Neuropsychiatry Clin Neurosci case reports).

Vaccine Development and Testing

"Iran hopes to defeat COVID with home-grown crop of vaccines – *Nature* talks to vaccine developer Kayhan Azadmanesh about efforts in Iran to develop ten or more COVID jabs, two of which have been approved for use" (Nature).

"A Texas lab performs crucial testing for Pfizer's COVID vaccine" (NPR).

"Covid-19 vaccines flirted with perfection at first. Reality is more complicated" (STAT).

Hesitancy and Refusal

"Vaccine refusers risk compassion fatigue – After the horrors that health-care workers have endured during the pandemic, many are struggling to sympathize with people who won't protect themselves" (Atlantic).

"'I'm still not planning to get it': FDA approval not swaying some vaccine holdouts – Skeptics who were waiting on regulators now say they have new doubts" (WP).

Special Reports and Other Resources

PIIE: How COVID-19 vaccine supply chains emerged in the midst of a pandemic (August 2021)

> "Many months after COVID-19 vaccines were first authorized for public use, still limited supplies could only partially reduce the devastating loss of life and economic costs caused by the pandemic. Could additional vaccine doses have been manufactured more quickly some other way? Would alternative policy choices have made a difference? This paper provides a simple analytical framework through which to view the contours of the vaccine value chain. It then creates a new database that maps the COVID-19 vaccines of Pfizer/BioNTech, Moderna, AstraZeneca/Oxford, Johnson & Johnson, Novavax, and CureVac to the product- and location-specific manufacturing supply chains that emerged in 2020 and 2021. It describes the choppy process through which dozens of other companies at nearly 100 geographically distributed facilities came together to scale up global manufacturing. The paper catalogues major pandemic policy initiatives—such as the United States' Operation Warp Speed—that are likely to have affected the timing and formation of those vaccine supply chains. Given the data, a final section identifies further questions for researchers and policymakers."

Journal Articles

Hospitalizations

MMWR: SARS-CoV-2 Infections and Hospitalizations Among Persons Aged ≥16 Years, by Vaccination Status — Los Angeles County, California, May 1–July 25, 2021 (27 August 2021)

> "What is already known about this topic? Although COVID-19 vaccines are highly effective, some fully vaccinated persons will be infected with SARS-CoV-2.
>
> What is added by this report? During May 1–July 25, 2021, among 43,127 SARS-CoV-2 infections in residents of Los Angeles County, California, 10,895 (25.3%) were in fully vaccinated persons, 1,431 (3.3%) were in partially vaccinated persons, and 30,801 (71.4%) were in unvaccinated persons. On July 25, infection and hospitalization rates among unvaccinated persons were 4.9 and 29.2 times, respectively, those in fully vaccinated persons. In July, when the Delta variant was predominant, cycle threshold values were similar for unvaccinated, partially vaccinated, and vaccinated persons.
>
> What are the implications for public health practice? Efforts to enhance COVID-19 vaccination coverage, in coordination with other prevention strategies, are critical to preventing COVID-19–related hospitalizations and deaths."

MMWR: New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status — New York, May 3–July 25, 2021 (27 August 2021)

> "What is already known about this topic? Real-world studies of population-level vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection and COVID-19 hospitalizations are limited in the United States.
>
> What is added by this report? During May 3–July 25, 2021, the overall age-adjusted vaccine effectiveness against hospitalization in New York was relatively stable (91.9%–95.3%). The overall age-adjusted vaccine effectiveness against infection for all New York adults declined from 91.7% to 79.8%.
>
> What are the implications for public health practice? These findings support the implementation of multicomponent approach to controlling the pandemic, centered on vaccination, as well as other prevention strategies such as masking and physical distancing."

MMWR: Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults — United States, March–July 2021 (27 August 2021)

> "What is already known about this topic? COVID-19 mRNA vaccines provide strong protection against severe COVID-19; however, the duration of protection is uncertain.
>
> What is added by this report? Among 1,129 patients who received 2 doses of a mRNA vaccine, no decline in vaccine effectiveness against COVID-19 hospitalization was observed

over 24 weeks. Vaccine effectiveness was 86% 2–12 weeks after vaccination and 84% at 13–24 weeks. Vaccine effectiveness was sustained among groups at risk for severe COVID-19.

What are the implications for public health practice? mRNA vaccine effectiveness against COVID-19–associated hospitalizations was sustained over 24 weeks; ongoing monitoring is needed as new SARS-CoV-2 variants emerge. To reduce hospitalization, all eligible persons should be offered COVID-19 vaccination."

MMWR: Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021 (27 August 2021)

"What is already known about this topic? Early observational studies among nursing home residents showed mRNA vaccines to be 53% to 92% effective against SARS-CoV-2 infection.

What is added by this report? Two doses of mRNA vaccines were 74.7% effective against infection among nursing home residents early in the vaccination program (March–May 2021). During June–July 2021, when B.1.617.2 (Delta) variant circulation predominated, effectiveness declined significantly to 53.1%.

What are the implications for public health practice? Multicomponent COVID-19 prevention strategies, including vaccination of nursing home staff members, residents, and visitors, are critical. An additional dose of COVID-19 vaccine might be considered for nursing home and long-term care facility residents to optimize a protective immune response."

Safety and Effectiveness

NEJM: Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting (25 August 2021)

"Background: Preapproval trials showed that messenger RNA (mRNA)-based vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a good safety profile, yet these trials were subject to size and patient-mix limitations. An evaluation of the safety of the BNT162b2 mRNA vaccine with respect to a broad range of potential adverse events is needed.

Methods: We used data from the largest health care organization in Israel to evaluate the safety of the BNT162b2 mRNA vaccine. For each potential adverse event, in a population of persons with no previous diagnosis of that event, we individually matched vaccinated persons to unvaccinated persons according to sociodemographic and clinical variables. Risk ratios and risk differences at 42 days after vaccination were derived with the use of the Kaplan-Meier estimator. To place these results in context, we performed a similar analysis

involving SARS-CoV-2-infected persons matched to uninfected persons. The same adverse events were studied in the vaccination and SARS-CoV-2 infection analyses.

Results: In the vaccination analysis, the vaccinated and control groups each included a mean of 884,828 persons. Vaccination was most strongly associated with an elevated risk of myocarditis (risk ratio, 3.24; 95% confidence interval [CI], 1.55 to 12.44; risk difference, 2.7 events per 100,000 persons; 95% CI, 1.0 to 4.6), lymphadenopathy (risk ratio, 2.43; 95% CI, 2.05 to 2.78; risk difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3), appendicitis (risk ratio, 1.40; 95% CI, 1.02 to 2.01; risk difference, 5.0 events per 100,000 persons; 95% CI, 0.3 to 9.9), and herpes zoster infection (risk ratio, 1.43; 95% CI, 1.20 to 1.73; risk difference, 15.8 events per 100,000 persons; 95% CI, 8.2 to 24.2). SARS-CoV-2 infection was associated with a substantially increased risk of myocarditis (risk ratio, 18.28; 95% CI, 3.95 to 25.12; risk difference, 11.0 events per 100,000 persons; 95% CI, 5.6 to 15.8) and of additional serious adverse events, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia.

Conclusions: In this study in a nationwide mass vaccination setting, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection."

Epidemiol Infect: SARS-CoV-2 Immunogenicity in individuals infected before and after COVID-19 vaccination: Israel, January-March 2021 (17 August 2021)

"Of approximately 1,500 employees, 725 received at least one dose of vaccine and were tested at least once post-vaccination. Of these, 25 had evidence of pre-vaccination infection and 35 had evidence of infection post-dose 1, of which 32 before they were eligible for dose 2. These 32 individuals did not receive dose 2 as they were no longer eligible owing to their infected status. Not all these patients were tested twice. Of the 541 individuals tested 15-35 days post dose 1, 96.9% had detectable antibodies and 99.8% of those tested 41-65 days post dose 1 had detectable antibodies….

Our study shows that when it comes to vaccinating infected individuals, the sequence of events matters. Individuals in our cohort infected postvaccination had IgG titers at 21 and 50 days similar to those never infected who received the same number of doses and much lower than those infected pre-vaccination. These data suggest that individuals infected after a single dose of the BNT162b2vaccine should remain eligible for a second dose to ensure adequate protection levels. Although the sample size of this study was too small to warrant a policy change by itself, larger studies should be conducted to confirm or refute these results in order to change vaccine policy if needed."

Adverse Effects/Events

NEJM: Myocarditis after Covid-19 mRNA Vaccination (18 August 2021)

> Letter to the editor: "Here, we report two cases of histologically confirmed myocarditis after Covid-19 mRNA vaccination…. In these two adult cases of histologically confirmed, fulminant myocarditis that had developed within 2 weeks after Covid-19 vaccination, a direct causal relationship cannot be definitively established because we did not perform testing for viral genomes or autoantibodies in the tissue specimens. However, no other causes were identified by PCR assay or serologic examination."

Lancet Infect Dis: Bell's palsy following vaccination with mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines: a case series and nested case-control study (16 August 2021)

> "Background: Bell's palsy is a rare adverse event reported in clinical trials of COVID-19 vaccines. However, to our knowledge no population-based study has assessed the association between the inactivated SARS-CoV-2 vaccines and Bell's palsy. The aim of this study was to evaluate the risk of Bell's palsy after BNT162b2 and CoronaVac vaccination.
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> Methods: In this case series and nested case-control study done in Hong Kong, we assessed the risk of Bell's palsy within 42 days following vaccination with BNT162b2 (Fosun-BioNTech [equivalent to Pfizer-BioNTech]) or CoronaVac (from Sinovac Biotech, Hong Kong) using data from voluntary surveillance reporting with the Hospital Authority, the COVID-19 Vaccine Adverse Event Online Reporting system for all health-care professionals, and the Hospital Authority's territory-wide electronic health records from the Clinical Data Analysis and Reporting System. We described reported cases of Bell's palsy among vaccine recipients (aged 18-110 years for CoronaVac and aged 16-110 years for BNT162b2). We compared the estimated age-standardised incidence of clinically confirmed cases among individuals who had received the CoronaVac or BNT162b2 vaccination (up to 42 days before presentation) with the background incidence in the population. A nested case-control study was also done using conditional logistic regression to estimate the odds ratio (OR) for risk of Bell's palsy and vaccination. Cases and controls were matched (1:4) by age, sex, admission setting, and admission date.
>
> Findings: Between February 23 and May 4, 2021, 451 939 individuals received the first dose of CoronaVac and 537 205 individuals received the first dose of BNT162b2. 28 clinically confirmed cases of Bell's palsy were reported following CoronaVac and 16 cases were reported following BNT162b2. The age-standardised incidence of clinically confirmed Bell's palsy was 66·9 cases per 100 000 person-years (95% CI 37·2 to 96·6) following CoronaVac vaccination and 42·8 per 100 000 person-years (19·4 to 66·1) for BNT162b2 vaccination. The age-standardised difference for the incidence compared with the background population was 41·5 (95% CI 11·7 to 71·4) for CoronaVac and 17·0 (-6·6 to 40·6) for BNT162b2, equivalent to an additional 4·8 cases per 100 000 people vaccinated for CoronaVac and 2·0

cases per 100 000 people vaccinated for BNT162b2. In the nested case-control analysis, 298 cases were matched to 1181 controls, and the adjusted ORs were 2·385 (95% CI 1·415 to 4·022) for CoronaVac and 1·755 (0·886 to 3·477) for BNT162b2.

Interpretation: Our findings suggest an overall increased risk of Bell's palsy after CoronaVac vaccination. However, the beneficial and protective effects of the inactivated COVID-19 vaccine far outweigh the risk of this generally self-limiting adverse event. Additional studies are needed in other regions to confirm our findings."

Impact

Health Aff: Vaccinations Against COVID-19 May Have Averted Up To 140,000 Deaths In The United States (18 August 2021)

"COVID-19 vaccination campaigns continue in the United States, with the expectation that vaccines will slow transmission of the virus, save lives, and enable a return to normal life in due course. However, the extent to which faster vaccine administration has affected COVID-19-related deaths is unknown. We assessed the association between US state-level vaccination rates and COVID-19 deaths during the first five months of vaccine availability. We estimated that by May 9, 2021, the US vaccination campaign was associated with a reduction of 139,393 COVID-19 deaths. The association varied in different states. In New York, for example, vaccinations led to an estimated 11.7 fewer COVID-19 deaths per 10,000, whereas Hawaii observed the smallest reduction, with an estimated 1.1 fewer deaths per 10,000. Overall, our analysis suggests that the early COVID-19 vaccination campaign was associated with reductions in COVID-19 deaths. As of May 9, 2021, reductions in COVID-19 deaths associated with vaccines had translated to value of statistical life benefit ranging between $625 billion and $1.4 trillion."

Science: Vaccine nationalism and the dynamics and control of SARS-CoV-2 (17 August 2021)

"Vaccines provide powerful tools to mitigate the enormous public health and economic costs that the ongoing SARS-CoV-2 pandemic continues to exert globally, yet vaccine distribution remains unequal among countries. To examine the potential epidemiological and evolutionary impacts of 'vaccine nationalism', we extend previous models to include simple scenarios of stockpiling between two regions. In general, when vaccines are widely available and the immunity they confer is robust, sharing doses minimizes total cases across regions. A number of subtleties arise when the populations and transmission rates in each region differ, depending on evolutionary assumptions and vaccine availability. When the waning of natural immunity contributes most to evolutionary potential, sustained transmission in low access regions results in an increased potential for antigenic evolution, which may result in the emergence of novel variants that affect epidemiological characteristics globally. Overall, our results stress the importance of rapid equitable vaccine distribution for global control of the pandemic."

Intranasal Vaccines

Sci Transl Med: Intranasal ChAdOx1 nCoV-19/AZD1222 vaccination reduces viral shedding after SARS-CoV-2 D614G challenge in preclinical models (18 August 2021)

> "ChAdOx1 nCoV-19/AZD1222 is an approved adenovirus-based vaccine for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) currently being deployed globally. Previous studies in rhesus macaques revealed that intramuscular vaccination with ChAdOx1 nCoV-19/AZD1222 provided protection against pneumonia but did not reduce shedding of SARS-CoV-2 from the upper respiratory tract. Here, we investigated whether intranasally administered ChAdOx1 nCoV-19 reduces detection of virus in nasal swabs after challenging vaccinated macaques and hamsters with SARS-CoV-2 carrying a D614G mutation in the spike protein. Viral loads in swabs obtained from intranasally vaccinated hamsters were decreased compared to control hamsters, and no viral RNA or infectious virus was found in lung tissue after a direct challenge or after direct contact with infected hamsters. Intranasal vaccination of rhesus macaques resulted in reduced virus concentrations in nasal swabs and a reduction in viral loads in bronchoalveolar lavage and lower respiratory tract tissue. Intranasal vaccination with ChAdOx1 nCoV-19/AZD1222 reduced virus concentrations in nasal swabs in two different SARS-CoV-2 animal models, warranting further investigation as a potential vaccination route for COVID-19 vaccines."

mBio: Oral Bacteria Combined with an Intranasal Vaccine Protect from Influenza A Virus and SARS-CoV-2 Infection (17 August 2021)

> "The gut microbiota plays a critical role in the induction of adaptive immune responses to influenza virus infection. However, the role of nasal bacteria in the induction of the virus-specific adaptive immunity is less clear. Here, we found that disruption of nasal bacteria by intranasal application of antibiotics before influenza virus infection enhanced the virus-specific antibody response in a MyD88-dependent manner. Similarly, disruption of nasal bacteria by lysozyme enhanced antibody responses to intranasally administered influenza virus hemagglutinin (HA) vaccine in a MyD88-dependent manner, suggesting that intranasal application of antibiotics or lysozyme could release bacterial pathogen-associated molecular patterns (PAMPs) from disrupted nasal bacteria that act as mucosal adjuvants by activating the MyD88 signaling pathway. Since commensal bacteria in the nasal mucosal surface were significantly lower than those in the oral cavity, intranasal administration of HA vaccine alone was insufficient to induce the vaccine-specific antibody response. However, intranasal supplementation of cultured oral bacteria from a healthy human volunteer enhanced antibody responses to an intranasally administered HA vaccine. Finally, we demonstrated that oral bacteria combined with an intranasal vaccine protect from influenza virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Our results reveal the role of nasal bacteria in the induction of the virus-specific adaptive immunity and provide clues for developing better intranasal vaccines.

> IMPORTANCE Intranasal vaccination induces the nasal IgA antibody which is protective against respiratory viruses, such as influenza virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Therefore, understanding how mucosal immune responses are elicited following viral infection is important for developing better vaccines. Here, we focused on the role of nasal commensal bacteria in the induction of immune responses following influenza virus infection. To deplete nasal bacteria, we intranasally administered antibiotics to mice before influenza virus infection and found that antibiotic-induced disruption of nasal bacteria could release bacterial components which stimulate the virus-specific antibody responses. Since commensal bacteria in nasal mucosa were significantly lower than those in the oral cavity, intranasal administration of split virus vaccine alone was insufficient to induce the vaccine-specific antibody response. However, intranasal supplementation of cultured oral bacteria from a healthy human volunteer enhanced antibody responses to the intranasally administered vaccine. Therefore, both integrity and amounts of nasal bacteria may be critical for an effective intranasal vaccine."

Breakthrough Infections, Reinfections, and Coinfections

News in Brief

"Have you already had a breakthrough COVID infection? The question of what 'infection' means is just one of the riddles posed by the late-stage pandemic" (New Yorker).

"Breakthrough COVID infections add even more chaos to school's start in 2021" (NPR).

"Being fully vaccinated against COVID-19 significantly decreased the probability of virus culture positivity in breakthrough cases versus cases in unvaccinated healthcare workers" (CIDRAP; see also: medRxiv preprint).

Journal Articles

Clin Infect Dis: Post-vaccination COVID-19: A case-control study and genomic analysis of 119 breakthrough infections in partially vaccinated individuals (19 August 2021)

> "Background: Post-vaccination infections challenge the control of the COVID-19 pandemic.
>
> Methods: We matched 119 cases of post-vaccination SARS-CoV-2 infection with BNT162b2 mRNA, or ChAdOx1 nCOV-19, to 476 unvaccinated patients with COVID-19 (Sept 2020-March 2021), according to age and sex. Differences in 60-day all-cause mortality, hospital admission, and hospital length of stay were evaluated. Phylogenetic, single nucleotide

polymorphism (SNP) and minority variant allele (MVA) full genome sequencing analysis was performed.

Results: 116/119 cases developed COVID-19 post first vaccination dose (median 14 days, IQR 9 - 24 days). Overall, 13/119 (10·9%) cases and 158/476 (33·2%) controls died (p<0.001), corresponding to 4·5 number needed to treat (NNT). Multivariably, vaccination was associated with 69·3% (95%CI 45·8 - 82·6) relative risk (RR) reduction in mortality. Similar results were seen in subgroup analysis for patients with infection onset ≥14 days after first vaccination (RR reduction 65·1%, 95%CI 27·2 - 83·2, NNT 4·5), and across vaccine subgroups (BNT162b2: RR reduction 66%, 95%CI 34·9 - 82·2, NNT 4·7, ChAdOx1: RR reduction 78·4%, 95%CI 30·4 - 93·3, NNT 4·1). Hospital admissions (OR 0·80, 95%CI 0·51 - 1·28), and length of stay (-1·89 days, 95%CI -4·57 - 0·78) were lower for cases, while Ct values were higher (30·8 versus 28·8, p = 0.053). B.1.1.7 was the predominant lineage in cases (100/108, 92.6%) and controls (341/446, 76.5%). Genomic analysis identified one post-vaccination case harboring the E484K vaccine escape mutation (B.1.525 lineage).

Conclusions: Previous vaccination reduces mortality when B.1.1.7 is the predominant lineage. No significant lineage-specific genomic changes during phylogenetic, SNP and MVA analysis were detected."

NEJM: Breakthrough Infections in BNT162b2-Vaccinated Health Care Workers (18 August 2021)

Letter to the editor in response to Hacisueyman et al.: "At our institution, 1137 health care workers were fully vaccinated with BNT162b2. Of these, 4 immunocompetent women (0.35%) had breakthrough infections…. The health care workers at our institution had only mild symptoms but high viral loads (cycle thresholds of <25) and prolonged viral shedding up to 32 days after diagnosis. We performed a genomic characterization of the spike protein variants (delHV69/70, N501Y, A570D, D614G, and P681H), and all strains were classified as the B.1.1.7 (or alpha) variant."

Emerg Infect Dis: *Bordetella hinzii* pneumonia and bacteremia in a patient with SARS-CoV-2 infection (13 August 2021)

"Patients with severe acute respiratory syndrome coronavirus 2 infection may have bacterial co-infections, including pneumonia and bacteremia. *Bordetella hinzii* infections are rare, may be associated with exposure to poultry, and have been reported mostly among immunocompromised patients. We describe *B. hinzii* pneumonia and bacteremia in a severe acute respiratory syndrome coronavirus 2 patient."

Treatments and Management

News in Brief

NIH treatment guidelines for severe COVID-19 now recommend IV sarilumab and tofacitinib can be used as alternatives to tocilizumab and baricitinib, respectively, if not unavailable or feasible to use (NIH).

"With no beds, hospitals ship patients to far-off cities" (AP).

"Monoclonal antibodies are free and effective against covid-19, but few people are getting them" (WP).

The FDA *really* doesn't want folks to self-medicate with ivermectin that they might get at the local co-op or veterinarian's office (FDA; see also: tweet).

Journal Articles

NEJM: Early Convalescent Plasma for High-Risk Outpatients with Covid-19 (18 August 2021)

> "Background: Early administration of convalescent plasma obtained from blood donors who have recovered from coronavirus disease 2019 (Covid-19) may prevent disease progression in acutely ill, high-risk patients with Covid-19.
>
> Methods: In this randomized, multicenter, single-blind trial, we assigned patients who were being treated in an emergency department for Covid-19 symptoms to receive either one unit of convalescent plasma with a high titer of antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or placebo. All the patients were either 50 years of age or older or had one or more risk factors for disease progression. In addition, all the patients presented to the emergency department within 7 days after symptom onset and were in stable condition for outpatient management. The primary outcome was disease progression within 15 days after randomization, which was a composite of hospital admission for any reason, seeking emergency or urgent care, or death without hospitalization. Secondary outcomes included the worst severity of illness on an 8-category ordinal scale, hospital-free days within 30 days after randomization, and death from any cause.
>
> Results: A total of 511 patients were enrolled in the trial (257 in the convalescent-plasma group and 254 in the placebo group). The median age of the patients was 54 years; the median symptom duration was 4 days. In the donor plasma samples, the median titer of SARS-CoV-2 neutralizing antibodies was 1:641. Disease progression occurred in 77 patients (30.0%) in the convalescent-plasma group and in 81 patients (31.9%) in the placebo group (risk difference, 1.9 percentage points; 95% credible interval, -6.0 to 9.8; posterior

probability of superiority of convalescent plasma, 0.68). Five patients in the plasma group and 1 patient in the placebo group died. Outcomes regarding worst illness severity and hospital-free days were similar in the two groups.

Conclusions: The administration of Covid-19 convalescent plasma to high-risk outpatients within 1 week after the onset of symptoms of Covid-19 did not prevent disease progression."

Ann Intern Med: Use of Hydroxychloroquine, Remdesivir, and Dexamethasone Among Adults Hospitalized With COVID-19 in the United States (17 August 2021)

"Background: Relatively little is known about the use patterns of potential pharmacologic treatments of COVID-19 in the United States.

Objective: To use the National COVID Cohort Collaborative (N3C), a large, multicenter, longitudinal cohort, to characterize the use of hydroxychloroquine, remdesivir, and dexamethasone, overall as well as across individuals, health systems, and time.

Design: Retrospective cohort study.

Setting: 43 health systems in the United States.

Participants: 137 870 adults hospitalized with COVID-19 between 1 February 2020 and 28 February 2021.

Measurements: Inpatient use of hydroxychloroquine, remdesivir, or dexamethasone.

Results: Among 137 870 persons hospitalized with confirmed or suspected COVID-19, 8754 (6.3%) received hydroxychloroquine, 29 272 (21.2%) remdesivir, and 53 909 (39.1%) dexamethasone during the study period. Since the release of results from the RECOVERY (Randomised Evaluation of COVID-19 Therapy) trial in mid-June, approximately 78% to 84% of people who have had invasive mechanical ventilation have received dexamethasone or other glucocorticoids. The use of hydroxychloroquine increased during March 2020, peaking at 42%, and started declining by April 2020. By contrast, remdesivir and dexamethasone use gradually increased over the study period. Dexamethasone and remdesivir use varied substantially across health centers (intraclass correlation coefficient, 14.2% for dexamethasone and 84.6% for remdesivir).

Limitation: Because most N3C data contributors are academic medical centers, findings may not reflect the experience of community hospitals.

Conclusion: Dexamethasone, an evidence-based treatment of COVID-19, may be underused among persons who are mechanically ventilated. The use of remdesivir and dexamethasone varied across health systems, suggesting variation in patient case mix, drug access, treatment protocols, and quality of care."

Remdesivir

Clin Infect Dis: Optimal timing of remdesivir initiation in hospitalized COVID-19 patients administered with dexamethasone (22 August 2021)

> "Background: Evidence is lacking about any additional benefits of introducing remdesivir on top of dexamethasone, and the optimal timing of initiation.
>
> Methods: In a territory-wide cohort of 10,445 COVID-19 patients from Hong Kong who were hospitalized between 21st January 2020 and 31st January 2021, 1544 patients had received dexamethasone during hospitalization. Exposure group consisted of patients who had initiated remdesivir prior to dexamethasone (n=93), or co-initiated the two drugs simultaneously (n=373); whereas non-exposure group included patients who were given remdesivir after dexamethasone (n=149), or those without remdesivir use (n=929). Multiple imputation and inverse probability of treatment weighting for propensity score were applied and hazard ratios (HR) of event outcomes were estimated using Cox regression models.
>
> Results: Time to clinical improvement (HR=1.23, 95%CI 1.02-1.49, p=0.032) and positive IgG antibody (HR=1.22, 95%CI 1.02-1.46, p=0.029) were significantly shorter in the exposure group than that of non-exposure. The exposure group had a shorter hospital length of stay by 2.65 days among survivors, lower WHO clinical progression scale scores from five days of follow-up onwards, lower risks of in-hospital death (HR=0.59, 95%CI 0.36-0.98, p=0.042) and composite outcomes; and without experiencing an increased risk of ARDS. Differences in the cumulative direct medical costs between groups were no longer significant from 17 days of follow-up onwards.
>
> Conclusions: Initiation of remdesivir prior to or simultaneously with dexamethasone was associated with significantly shorter time to clinical improvement and positive IgG antibody, lower risk of in-hospital death, in addition to shorter length of hospital stay in patients with moderate COVID-19."

Clin Infect Dis: Remdesivir and Mortality in Patients with COVID-19 (19 August 2021)

> "Background: The impact of remdesivir (RDV) on COVID-19 mortality is controversial, and the mortality effect in sub-groups of baseline disease severity has been incompletely explored. The purpose of this study was to assess the association of RDV with mortality in patients with COVID-19.
>
> Methods: In this retrospective cohort study we compared persons receiving RDV to persons receiving best supportive care (BSC). Patients hospitalized between 2/28/20 - 5/28/20 with laboratory confirmed SARS-CoV-2 infection were included when they developed COVID-19 pneumonia on chest radiography, and hypoxia requiring supplemental oxygen or SpO2 ≤ 94% on room air. The primary outcome was overall survival assessed with time-dependent

Cox proportional-hazards regression and multivariable adjustment, including calendar time, baseline patient characteristics, corticosteroid use and effects for hospital.

Results: 1,138 patients were enrolled including 286 who received RDV, and 852 treated with BSC, 400 of whom received hydroxychloroquine. Corticosteroids were used in 20.4% of the cohort (12.6% in RDV and 23% in BSC). In persons receiving RDV compared to those receiving BSC the HR (95%CI) for death was 0.46 (0.31 - 0.69) in the univariate model, p<0.001 and 0.60 (0.40 - 0.90) in the risk-adjusted model, p=0.014. In the sub-group of persons with baseline use of low-flow oxygen, the HR (95%CI) for death in RDV compared to BSC was 0.63 (0.39 - 1.00), p=0.049.

Conclusion: Treatment with RDV was associated with lower mortality compared to BSC. These findings remain the same in the subgroup with baseline use of low-flow oxygen."

Clin Infect Dis: Deconstructing the Treatment Effect of Remdesivir in the Adaptive COVID-19 Treatment Trial-1: Implications for Critical Care Resource Utilization (19 August 2021)

"Background: The Adaptive COVID-19 Treatment Trial-1 (ACTT-1) found that remdesivir therapy hastened recovery in patients hospitalized with COVID-19, but the pathway for this improvement was not explored. We investigated how the dynamics of clinical progression changed along 4 pathways: recovery, improvement in respiratory therapy requirement, deterioration in respiratory therapy requirement, and death.

Methods: We analyzed trajectories of daily ordinal severity scores reflecting oxygen requirements of 1051 patients hospitalized with COVID-19 who participated in ACTT-1. We developed competing risks models that estimate the effect of remdesivir therapy on cumulative incidence of clinical improvement and deterioration, and multistate models that utilize the entirety of each patient's clinical course to characterize the effect of remdesivir on progression along the 4 pathways above.

Results: Based on a competing risks analysis, remdesivir reduced clinical deterioration (hazard ratio, 0.73; 95% CI, 0.59-0.91) and increased clinical improvement (hazard ratio, 1.22; 95% CI, 1.08, 1.39) relative to baseline. Our multistate models indicate that remdesivir inhibits worsening to ordinal scores of greater clinical severity among patients on room air or low-flow oxygen (hazard ratio, 0.74; 95% CI, 0.57-0.94) and among patients receiving mechanical ventilation or high-flow oxygen/noninvasive positive-pressure ventilation (hazard ratio, 0.73; 95% CI, 0.53-1.00) at baseline. We also find that remdesivir reduces expected intensive care respiratory therapy utilization among patients not mechanically ventilated at baseline.

Conclusions: Remdesivir speeds time to recovery by preventing worsening to clinical states that would extend the course of hospitalization and increase intensive respiratory support, thereby reducing the overall demand for hospital care."

Biomarkers

JAC Antimicrob Resist: Evaluation of procalcitonin-guided antimicrobial stewardship in patients admitted to hospital with COVID-19 pneumonia (20 August 2021)

> "Background: Procalcitonin is a biomarker that may be able to identify patients with COVID-19 pneumonia who do not require antimicrobials for bacterial respiratory tract co-infections.
>
> Objectives: To evaluate the safety and effectiveness of a procalcitonin-guided algorithm in rationalizing empirical antimicrobial prescriptions in non-critically ill patients with COVID-19 pneumonia.
>
> Methods: Retrospective, single-site, cohort study in adults hospitalized with confirmed or suspected COVID-19 pneumonia and receiving empirical antimicrobials for potential bacterial respiratory tract co-infection. Regression models were used to compare the following outcomes in patients with and without procalcitonin testing within 72 h of starting antimicrobials: antimicrobial consumption (DDD); antimicrobial duration; a composite safety outcome of death, admission to HDU/ICU or readmission to hospital within 30 days; and length of admission. Procalcitonin levels of ≤0.25 ng/L were interpreted as negatively predictive of bacterial co-infection. Effects were expressed as ratios of means (ROM) or prevalence ratios (PR) accordingly.
>
> Results: 259 patients were included in the final analysis. Antimicrobial use was lower in patients who had procalcitonin measured within 72 h of starting antimicrobials: mean antimicrobial duration 4.4 versus 5.4 days, adjusted ROM 0.7 (95% CI 0.6–0.9); mean antimicrobial consumption 6.8 versus 8.4 DDD, adjusted ROM 0.7 (95% CI 0.6–0.8). Both groups had similar composite safety outcomes (adjusted PR 0.9; 95% CI 0.6–1.3) and lengths of admission (adjusted ROM 1.3; 95% CI 0.9–1.6).
>
> Conclusions: A procalcitonin-guided algorithm may allow for the safe reduction of antimicrobial usage in hospitalized non-critically ill patients with COVID-19 pneumonia."

Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues

News in Brief

"Man shot 6 times waits more than a week for surgery after hospital is overwhelmed by covid" (WP).

Journal Articles

Anaesthesia: SARS-CoV-2 infection and venous thromboembolism after surgery: an international prospective cohort study (24 August 2021)

> "SARS-CoV-2 has been associated with an increased rate of venous thromboembolism in critically ill patients. Since surgical patients are already at higher risk of venous thromboembolism than general populations, this study aimed to determine if patients with peri-operative or prior SARS-CoV-2 were at further increased risk of venous thromboembolism. We conducted a planned sub-study and analysis from an international, multicentre, prospective cohort study of elective and emergency patients undergoing surgery during October 2020. Patients from all surgical specialties were included. The primary outcome measure was venous thromboembolism (pulmonary embolism or deep vein thrombosis) within 30 days of surgery. SARS-CoV-2 diagnosis was defined as peri-operative (7 days before to 30 days after surgery); recent (1-6 weeks before surgery); previous (≥7 weeks before surgery); or none. Information on prophylaxis regimens or pre-operative anti-coagulation for baseline comorbidities was not available. Postoperative venous thromboembolism rate was 0.5% (666/123,591) in patients without SARS-CoV-2; 2.2% (50/2317) in patients with peri-operative SARS-CoV-2; 1.6% (15/953) in patients with recent SARS-CoV-2; and 1.0% (11/1148) in patients with previous SARS-CoV-2. After adjustment for confounding factors, patients with peri-operative (adjusted odds ratio 1.5 (95%CI 1.1-2.0)) and recent SARS-CoV-2 (1.9 (95%CI 1.2-3.3)) remained at higher risk of venous thromboembolism, with a borderline finding in previous SARS-CoV-2 (1.7 (95%CI 0.9-3.0)). Overall, venous thromboembolism was independently associated with 30-day mortality (5.4 (95%CI 4.3-6.7)). In patients with SARS-CoV-2, mortality without venous thromboembolism was 7.4% (319/4342) and with venous thromboembolism was 40.8% (31/76). Patients undergoing surgery with peri-operative or recent SARS-CoV-2 appear to be at increased risk of postoperative venous thromboembolism compared with patients with no history of SARS-CoV-2 infection. Optimal venous thromboembolism prophylaxis and treatment are unknown in this cohort of patients, and these data should be interpreted accordingly."

JAMA Netw Open: Public Perspectives on Decisions About Emergency Care Seeking for Care Unrelated to COVID-19 During the COVID-19 Pandemic (19 August 2021)

> "Question: What do people prioritize when deciding whether to present to the emergency department during the COVID-19 pandemic for care unrelated to COVID-19?
>
> Findings: In this survey study of 933 US adults, we found that 16.9% and 25.5% of individuals confronted with scenarios consistent with myocardial infarction or appendicitis, respectively, prioritized avoidance of COVID-19 exposure in the emergency department over seeking appropriate care. Sociodemographics, political affiliations, and personal

knowledge, attitudes, and beliefs regarding COVID-19 were not factors associated with decision-making regarding emergency care seeking.

Meaning: These findings suggest that health care systems and public health organizations should develop effective communications for patients and the community at large that reassure and encourage appropriate, timely health care for critical needs, not only during the ongoing COVID-19 pandemic, but also for future infectious outbreaks and other scenarios that could promote maladaptive pathogen-avoidance behaviors."

JAMA Otolaryngol Head Neck Surg: Total Laryngectomy Volume During the COVID-19 Pandemic: Looking for Evidence of Stage Migration (19 August 2021)

Research letter: "This cohort study examines the association of the COVID-19 pandemic with total laryngectomy volumes among patients in Ontario, Canada….

The current study did not show an increase in laryngectomy surgical volume during the COVID-19 pandemic. This study provides early, real-world evidence suggesting that Ontario's head and neck oncology response may have mitigated adverse health outcomes stemming from broader diagnostic and treatment delays. Care has been equitable during the pandemic compared with the prepandemic period, with no group disproportionately affected."

J Infect: Influenza and Anosmia: important prediction factors for severity and death of COVID-19 (18 August 2021)

"Objectives: To investigate the factors related to the severity and mo rtality of COVID-19 using big data-machine learning techniques.

Methods: This study included 8070 patients in South Korea diagnosed with COVID-19 between January and July 2020, and whose data were available from the National-Health-Insurance-Service.

Results: Machine-learning algorithms were performed to evaluate the effects of comorbidities on severity and mortality of COVID-19. The most common comorbidities of COVID-19 were pulmonary inflammation followed by hypertension. The model that best predicted severity was a neural network (AUC: 85.06%). The most important variable for predicting severity in the neural network model was a history of influenza (relative importance: 0.083). The model that best predicted mortality was the logistic regression elastic net (EN) model (AUC: 93.86%). The most important variables for mortality in the EN model were age (coefficient: 2.136) and anosmia (coefficient: -1.438).

Conclusions: In COVID-19 patients, influenza was found to be a major adverse factor in addition to old age and male. In addition, anosmia was found to be a major factor associated with lower severity and mortality. Therefore, in the current situation where

there is no adequate COVID-19 treatment at present, examining the patient's history of influenza vaccination and anosmia in addition to age and sex will be an important indicator for predicting the severity and mortality of COVID-19 patients."

Cancer Patients and Screening

Cancer: Changes in breast cancer screening rates among 32 community health centers during the COVID-19 pandemic (26 August 2021)

"Background: Breast cancer screening utilization steeply dropped at the start of the coronavirus disease 2019 (COVID-19) pandemic. However, the effects on breast cancer screening in lower income populations are unknown. This study examined changes in breast cancer screening rates (BCSRs) during the pandemic among 32 community health centers (CHCs) that provided health care to lower income populations.

Methods: Secondary data from 32 CHCs participating in an American Cancer Society grant program to increase breast cancer screening services were used. BCSRs were defined as the percentage of women aged 50 to 74 years who had a medical visit in the past 12 months (142,207 in 2018, 142,003 in 2019, and 150,630 in 2020) and received a screening mammogram within the last 27 months. BCSRs in July 2020, July 2019, and June 2018 were compared with screening rate ratios (SRRs) and corresponding 95% confidence intervals (CIs).

Results: BCSRs significantly rose by 18% between 2018 and 2019 (from 45.8% to 53.9%; SRR, 1.18; 95% CI, 1.17-1.18) and then declined by 8% between 2019 and 2020 (from 53.9% to 49.6%; SRR, 0.92; 95% CI, 0.92-0.93). If the 2018-2019 BCSR trends had continued through 2020, 63.3% of women would have been screened in 2020 in contrast to the 49.6% who were; this potentially translated into 47,517 fewer mammograms and 242 missed breast cancer diagnoses in this population.

Conclusions: In this study of 32 CHCs, BCSRs declined by 8% from July 2019 to 2020, and this reversed an 18% improvement between July 2018 and 2019. Declining BCSRs among CHCs during the COVID-19 pandemic call for policies to support and resources to identify women in need of screening."

JAMA Oncol: Association of Antineoplastic Therapy With Decreased SARS-CoV-2 Infection Rates in Patients With Cancer (19 August 2021)

"Question: Will patients with cancer treated with antineoplastic compounds associated with lower angiotensin-converting enzyme 2 (ACE2) expression exhibit lower SARS-CoV-2 infection rates?

Findings: In an in silico analysis of the Library of Integrated Network-Based Cellular Signatures database, 91 compounds were associated with gene downregulation of the ACE2

entry receptor for SARS-CoV-2, including mTOR/PI3K inhibitors and antimetabolites. Patients who received a potential ACE2-lowering antineoplastic exhibited a statistically significantly reduced SARS-CoV-2 positivity rate of 7.0% compared with 12.9% in patients who received other antineoplastic therapies.

Meaning: Potential ACE2-lowering antineoplastics, including mTOR/PI3K inhibitors and antimetabolites, may exhibit clinical anti–SARS-CoV-2 activity."

Long COVID / Post-COVID Period

News in Brief

"Researchers start new investigation into Long COVID core outcome set….This project, Post-COVID Condition Core Outcomes, will start by surveying people living with Post-COVID-19 condition, assess what outcomes matter and build a plan in two phases" (ISARIC; see also: study website).

Long Reads

"How does COVID-19 affect the brain? A troubling picture emerges. Researchers find that people who only suffered mild infections can be plagued with life-altering and sometimes debilitating cognitive deficits" (NG; may require free signup and login to read).

Journal Articles

Lancet: 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study (28 August 2021)

"Background: The full range of long-term health consequences of COVID-19 in patients who are discharged from hospital is largely unclear. The aim of our study was to comprehensively compare consequences between 6 months and 12 months after symptom onset among hospital survivors with COVID-19.

Methods: We undertook an ambidirectional cohort study of COVID-19 survivors who had been discharged from Jin Yin-tan Hospital (Wuhan, China) between Jan 7 and May 29, 2020. At 6-month and 12-month follow-up visit, survivors were interviewed with questionnaires on symptoms and health-related quality of life (HRQoL), and received a physical examination, a 6-min walking test, and laboratory tests. They were required to report their health-care use after discharge and work status at the 12-month visit. Survivors who had completed pulmonary function tests or had lung radiographic abnormality at 6 months

were given the corresponding tests at 12 months. Non-COVID-19 participants (controls) matched for age, sex, and comorbidities were interviewed and completed questionnaires to assess prevalent symptoms and HRQoL. The primary outcomes were symptoms, modified British Medical Research Council (mMRC) score, HRQoL, and distance walked in 6 min (6MWD). Multivariable adjusted logistic regression models were used to evaluate the risk factors of 12-month outcomes.

Findings: 1276 COVID-19 survivors completed both visits. The median age of patients was 59·0 years (IQR 49·0–67·0) and 681 (53%) were men. The median follow-up time was 185·0 days (IQR 175·0–198·0) for the 6-month visit and 349·0 days (337·0–361·0) for the 12-month visit after symptom onset. The proportion of patients with at least one sequelae symptom decreased from 68% (831/1227) at 6 months to 49% (620/1272) at 12 months (p<0·0001). The proportion of patients with dyspnoea, characterised by mMRC score of 1 or more, slightly increased from 26% (313/1185) at 6-month visit to 30% (380/1271) at 12-month visit (p=0·014). Additionally, more patients had anxiety or depression at 12-month visit (26% [331/1271] at 12-month visit vs 23% [274/1187] at 6-month visit; p=0·015). No significant difference on 6MWD was observed between 6 months and 12 months. 88% (422/479) of patients who were employed before COVID-19 had returned to their original work at 12 months. Compared with men, women had an odds ratio of 1·43 (95% CI 1·04–1·96) for fatigue or muscle weakness, 2·00 (1·48–2·69) for anxiety or depression, and 2·97 (1·50–5·88) for diffusion impairment. Matched COVID-19 survivors at 12 months had more problems with mobility, pain or discomfort, and anxiety or depression, and had more prevalent symptoms than did controls.

Interpretation: Most COVID-19 survivors had a good physical and functional recovery during 1-year follow-up, and had returned to their original work and life. The health status in our cohort of COVID-19 survivors at 12 months was still lower than that in the control population."

J Hosp Med: Continuing Cardiopulmonary Symptoms, Disability, and Financial Toxicity 1 Month After Hospitalization for Third-Wave COVID-19: Early Results From a US Nationwide Cohort (18 August 2021)

"Background: Patients discharged after COVID-19 report ongoing needs.

Objectives: To measure incident symptoms after COVID-19 hospitalization.

Design, setting, and participants: Preplanned early look at 1-month follow-up surveys from patients hospitalized August 2020 to January 2021 in NHLBI PETAL Network's Biology and Longitudinal Epidemiology: COVID-19 Observational (BLUE CORAL) study. English- or Spanish-speaking hospitalized adults without substantial pre-COVID-19 disability with a positive molecular test for SARS-CoV-2.

Results: Overall, 253 patients were hospitalized for a median of 5 days (interquartile range [IQR], 3-8), and had a median age of 60 years (IQR, 45-68). By race/ethnicity, 136 (53.8%) were non-Hispanic White, 23 (9.1%) were non-Hispanic Black, and 83 (32.8%) were Hispanic. Most (139 [54.9%]) reported a new or worsened cardiopulmonary symptom, and 16% (n = 39) reported new or increased oxygen use; 213 (84.2%) patients reported not feeling fully back to their pre-COVID-19 level of functioning. New limitations in activities of daily living were present in 130 (52.8%) patients. Financial toxicities, including job loss or change (49 [19.8%]), having a loved one take time off (93 [37.8%]), and using up one's savings (58 [23.2%]), were common. Longer lengths of hospital stay were associated with greater odds of 1-month cardiopulmonary symptoms (adjusted odds ratio [aOR], 1.82 per additional week in the hospital; 95% CI, 1.11-2.98) and new disability (aOR, 2.06; 95% CI, 1.21-3.53). There were not uniform demographic patterns of association.

Limitations: We prioritized patients' reports of their own incident problems over objective testing.

Conclusion: Patients who survived COVID-19 in the United States during late 2020/early 2021 still faced new burdens 1 month after hospital discharge."

Clin Infect Dis: Twelve-month systemic consequences of COVID-19 in patients discharged from hospital: a prospective cohort study in Wuhan, China (14 August 2021)

"Background: Follow-up study of Coronavirus disease 2019 (COVID-19) survivors has rarely been reported. We aimed to investigate longitudinal changes in the characteristics of COVID-19 survivors after discharge.

Methods and findings: A total of 594 COVID-19 survivors discharged from Tongji Hospital in Wuhan from February 10 to April 30, 2020 were included and followed up until May 17, 2021. Laboratory and radiological findings, pulmonary function tests, electrocardiogram, symptoms and signs were analyzed. 257 (51.2%) patients had at least one symptom at 3 months post-discharge, which decreased to 169 (40.0%) and 138 (28.4%) at 6-month and 12-month visit respectively. During follow-up period, insomnia, chest tightness, and fatigue were the most prevalent symptoms. Most laboratory parameters returned to normal, whereas increased incidence of abnormal liver and renal function and cardiovascular injury was evidenced after discharge. Fibrous stripes (213; 42.4%), pleural thickening and adhesions (188; 37.5%) and enlarged lymph nodes (120; 23.9%) were the most common radiographical findings at 3 months post-discharge. The abnormalities of pulmonary function included obstructive, restrictive, and mixed, which were 5.5%, 4.0%, 0.9% at 6 months post, and 1.9%, 4.7%, 0.2% at 12 months. Electrocardiogram abnormalities occurred in 256 (51.0%) patients at 3 months post-discharge, including arrhythmia, ST-T change and conduction block, which increased to 258 (61.1%) cases at 6-month visit and were maintained at high frequency (242;49.8%) at 12-month visit.

Conclusions: Physiological, laboratory, radiological or electrocardiogram abnormalities, particularly those related to renal, cardiovascular, liver functions are common in patients who recovered from COVID-19 up to 12months post-discharge."

J Infect: Long-term impact of COVID-19 associated acute respiratory distress syndrome (13 August 2021)

"Objectives: To determine the health status, exercise capacity, and health related quality of life (HRQoL) of COVID-19 associated acute respiratory distress syndrome (ARDS) survivors, 8 months after diagnosis.

Methods: All eligible patients were interviewed and underwent a physical examination, chest X-ray, and 6 min walk test (6MWT). Scales to evaluate post-traumatic stress disorder, depression, anxiety, and HRQoL were applied.

Results: Of 1295 patients, 365 suffered ARDS and 166 survived to hospital discharge. Five died after discharge and 48 were lost to follow-up. Of the 113 remaining patients, 81% had persistent symptoms. More than 50% of patients completed less than 80% of the theoretical distance on the 6MWT, 50% had an abnormal X-ray and 93% of patients developed psychiatric disorders. Mean SF-36 scores were worse than in the general population. After multivariate regression analysis, female sex, non-Caucasian race, and Charlson index>2 were independent risk factors for a worse mental health component summary score on the SF-36, and age was associated with a better prognosis. Female sex and chronic obstructive pulmonary disease were independently associated with a worse physical component summary score.

Conclusion: COVID-19 associated ARDS survivors have long-term consequences in health status, exercise capacity, and HRQoL. Strategies addressed to prevent these sequelae are needed."

Women's Health, Pregnancy, and Perinatal Care

Journal Articles

Clin Infect Dis: Incidence, Clinical Characteristics, and Risk Factors of SARS-CoV-2 Infection among Pregnant Individuals in the United States (14 August 2021)

"Background: Follow-up study of Coronavirus disease 2019 (COVID-19) survivors has rarely been reported. We aimed to investigate longitudinal changes in the characteristics of COVID-19 survivors after discharge.

Methods and findings: A total of 594 COVID-19 survivors discharged from Tongji Hospital in Wuhan from February 10 to April 30, 2020 were included and followed up until May 17, 2021. Laboratory and radiological findings, pulmonary function tests, electrocardiogram, symptoms and signs were analyzed. 257 (51.2%) patients had at least one symptom at 3 months post-discharge, which decreased to 169 (40.0%) and 138 (28.4%) at 6-month and 12-month visit respectively. During follow-up period, insomnia, chest tightness, and fatigue were the most prevalent symptoms. Most laboratory parameters returned to normal, whereas increased incidence of abnormal liver and renal function and cardiovascular injury was evidenced after discharge. Fibrous stripes (213; 42.4%), pleural thickening and adhesions (188; 37.5%) and enlarged lymph nodes (120; 23.9%) were the most common radiographical findings at 3 months post-discharge. The abnormalities of pulmonary function included obstructive, restrictive, and mixed, which were 5.5%, 4.0%, 0.9% at 6 months post, and 1.9%, 4.7%, 0.2% at 12 months. Electrocardiogram abnormalities occurred in 256 (51.0%) patients at 3 months post-discharge, including arrhythmia, ST-T change and conduction block, which increased to 258 (61.1%) cases at 6-month visit and were maintained at high frequency (242;49.8%) at 12-month visit.

Conclusions: Physiological, laboratory, radiological or electrocardiogram abnormalities, particularly those related to renal, cardiovascular, liver functions are common in patients who recovered from COVID-19 up to 12months post-discharge."

Breastfeeding and Lactation

Breastfeed Med: Detection of SARS-CoV-2-Specific IgA in the Human Milk of COVID-19 Vaccinated Lactating Health Care Workers (20 August 2021)

"Background: In 2019, a deadly virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), emerged. In December 2020, two mRNA-based COVID-19 vaccines were approved for use in the United States, which provide immunity to those receiving the vaccine. Maternally derived antibodies are a key element of infants' immunity. Certain vaccines given to pregnant and lactating mothers provide immunity to infants through transmission across the placenta, umbilical cord (IgG), and human milk (IgA). Human milk produced by mothers with a history of COVID-19 infection contains SARS-CoV-2 IgA and IgG. The purpose of this study is to determine whether SARS-CoV-2-specific immunoglobulins are found in human milk after the COVID-19 vaccination, and to characterize the types of immunoglobulins present.

Methods: This is a prospective observational study conducted at Shands Hospital, University of Florida, from December 2020 to March 2021. Twenty-two lactating health care workers who received the SARS-CoV-2 mRNA vaccine (Pfizer/BioNTech or Moderna) made up the sample group. Plasma and human milk were collected at three time points (prevaccination, post-first vaccine dose, and post-second vaccine dose). SARS-CoV-2-specific IgA and IgG in

human milk and in plasma were measured by enzyme-linked immunosorbent assay (ELISA). Maternal demographics were compiled.

Results: We found significant secretion of SARS-CoV-2-specific IgA and IgG in human milk and plasma after SARS-CoV-2 vaccination.

Conclusions: Our results show that the mRNA-based COVID-19 vaccines induce SARS-CoV-2-specific IgA and IgG secretion in human milk. Further studies are needed to determine the duration of this immune response, its capacity to neutralize the COVID-19 virus, the transfer of passive immunity to breastfeeding infants, and the potential therapeutic use of human milk IgA to combat SARS-CoV-2 infections and COVID-19."

Pediatrics: SARS-CoV-2 Antibodies in Breast Milk After Vaccination (18 August 2021)

"BACKGROUND AND OBJECTIVES: Passive and active immunity transfer through human milk (HM) constitutes a key element in the infant's developing immunity. Certain infectious diseases and vaccines have been described to induce changes in the immune components of HM.

METHODS: We conducted a prospective cohort single institution study from February 2 to April 4, 2021. Women who reported to be breastfeeding at the time of their COVID-19 vaccination were invited to participate. Blood and milk samples were collected on day 14 after their second dose of vaccine. IgG antibodies against nucleocapsid protein as well as IgG and IgM antibodies against the spike 1 protein receptor-binding domain (RBD) were analyzed in both serum and HM. The latter was tested for IgA, IgM, and IgG antibodies against SARSCoV-2.

RESULTS: Most of the participants, ie, 94%, received the BNT162b2 mRNA COVID-19 vaccine and 6% the mRNA-1273 COVID-19 vaccine. The mean serum concentration of IgG antibodies against the SARS-CoV-2 spike protein RBD in vaccinated individuals was 3379.6±1639.5 BAU/mL. All vaccinated study participants had IgG antibodies and 89% of them IgA antibodies against SARS-CoV-2 in their milk. IgA and IgG antibody concentrations in the milk of mothers who were breastfeeding ≥24 months were significantly higher than in mothers with breastfeeding periods <24 months (P <.001).

CONCLUSIONS: We found a clear association between COVID-19 vaccination and specific immunoglobulin concentrations in HM. This effect was more pronounced when lactation periods exceeded 23 months. The influence of the lactation period on immunoglobulins was specific and independent of other variables."

JAMA Netw Open: Short-term Reactions Among Pregnant and Lactating Individuals in the First Wave of the COVID-19 Vaccine Rollout (17 August 2021)

> Research letter: "This cohort study investigates short-term reactions associated with COVID-19 vaccines among pregnant and lactating individuals vs individuals neither pregnant nor lactating but planning pregnancy….
>
> This large prospective cohort study found that COVID-19 vaccines were well-tolerated among individuals who were pregnant, lactating, or planning pregnancy. A strength of this study was the ability to compare vaccine reactions and perceptions in pregnant and lactating individuals vs individuals of similar age and fertility intentions who were neither pregnant nor lactating. Vaccination reactions for day 1 were similar among groups and comparable with findings among pregnant individuals previously reported. All groups reported increased reactions following dose 2 of BNT162b2 and mRNA-1273 vaccines."

Pediatric Population

News in Brief

"US pediatric COVID-19 cases now match winter surge" (CIDRAP).

"Among children, older teens are seeing the highest Covid-19 case rates" (CNN).

Back to School

"Many kids have missed routine vaccines, worrying doctors as school starts" (NPR).

"Add kids' pandemic anxiety to list of back-to-school concerns, experts say – Adults urged to model self-care, foster resilience as children return to school" (Medpage).

Supporting Kids

Commentary: "Use HIV's lessons to help children orphaned by COVID-19 – Young people who have lost parents to the pandemic need urgent support and long-term study to avert the cascade of adversity that can follow. Decades of research into the HIV epidemic provide a solid foundation" (Nature).

Special Reports and Other Resources

ASPR TRACIE: Technical Assistance Request: Pediatric Surge Considerations [pdf] (12 August 2021)

> "The ASPR TRACIE Team reviewed material on our COVID-19 Resources page and searched for additional resources in our Pediatric/Children Topic Collection and Pediatric Crisis Standards of Care Resources technical assistance (TA) response document. Section I of this

TA response document includes general considerations related to pediatric surge capacity, capability, management, and guidance. Section II provides healthcare coalition (HCC)-related resources and considerations. Section III includes resources that focus on operational considerations. Section IV provides resources and considerations specific to telehealth. Section V includes links to operationally focused resources and VI highlights additional related resources."

Document includes links and other resources.

Journal Articles

Pediatrics: Thirty-Day Outcomes of Children and Adolescents With COVID-19: An International Experience (20 August 2021)

"Objectives: To characterize the demographics, comorbidities, symptoms, in-hospital treatments, and health outcomes among children and adolescents diagnosed or hospitalized with coronavirus disease 2019 (COVID-19) and to compare them in secondary analyses with patients diagnosed with previous seasonal influenza in 2017-2018.

Methods: International network cohort using real-world data from European primary care records (France, Germany, and Spain), South Korean claims and US claims, and hospital databases. We included children and adolescents diagnosed and/or hospitalized with COVID-19 at age <18 between January and June 2020. We described baseline demographics, comorbidities, symptoms, 30-day in-hospital treatments, and outcomes including hospitalization, pneumonia, acute respiratory distress syndrome, multisystem inflammatory syndrome in children, and death.

Results: A total of 242 158 children and adolescents diagnosed and 9769 hospitalized with COVID-19 and 2 084 180 diagnosed with influenza were studied. Comorbidities including neurodevelopmental disorders, heart disease, and cancer were more common among those hospitalized with versus diagnosed with COVID-19. Dyspnea, bronchiolitis, anosmia, and gastrointestinal symptoms were more common in COVID-19 than influenza. In-hospital prevalent treatments for COVID-19 included repurposed medications (<10%) and adjunctive therapies: systemic corticosteroids (6.8%-7.6%), famotidine (9.0%-28.1%), and antithrombotics such as aspirin (2.0%-21.4%), heparin (2.2%-18.1%), and enoxaparin (2.8%-14.8%). Hospitalization was observed in 0.3% to 1.3% of the cohort diagnosed with COVID-19, with undetectable (n < 5 per database) 30-day fatality. Thirty-day outcomes including pneumonia and hypoxemia were more frequent in COVID-19 than influenza.

Conclusions: Despite negligible fatality, complications including hospitalization, hypoxemia, and pneumonia were more frequent in children and adolescents with COVID-19 than with influenza. Dyspnea, anosmia, and gastrointestinal symptoms could help differentiate

diagnoses. A wide range of medications was used for the inpatient management of pediatric COVID-19."

JAMA Pediatr: Association of Age and Pediatric Household Transmission of SARS-CoV-2 Infection (16 August 2021)

"Question: Are there differences in the odds of household transmission of SARS-CoV-2 by younger children compared with older children?

Findings: In this cohort study of 6280 households with pediatric index cases, the adjusted odds of household transmission by children aged 0 to 3 years was 1.43 compared with children aged 14 to 17 years.

Meaning: Younger children may have greater risk of transmitting SARS-CoV-2 to caregivers and siblings in the household than older children."

Pediatrics: Acute Respiratory Illnesses in Children in the SARS-CoV-2 Pandemic: Prospective Multicenter Study (02 August 2021)

"Objectives: Nonpharmaceutical interventions against coronavirus disease 2019 likely have a role in decreasing viral acute respiratory illnesses (ARIs). We aimed to assess the frequency of respiratory syncytial virus (RSV) and influenza ARIs before and during the coronavirus disease 2019 pandemic.

Methods: This study was a prospective, multicenter, population-based ARI surveillance, including children seen in the emergency departments and inpatient settings in 7 US cities for ARI. Respiratory samples were collected and evaluated by molecular testing. Generalized linear mixed-effects models were used to evaluate the association between community mitigation and number of eligible and proportion of RSV and influenza cases.

Results: Overall, 45 759 children were eligible; 25 415 were enrolled and tested; 25% and 14% were RSV-positive and influenza-positive, respectively. In 2020, we noted a decrease in eligible and enrolled ARI subjects after community mitigation measures were introduced, with no RSV or influenza detection from April 5, 2020, to April 30, 2020. Compared with 2016-2019, there was an average of 10.6 fewer eligible ARI cases per week per site and 63.9% and 45.8% lower odds of patients testing positive for RSV and influenza, respectively, during the 2020 community mitigation period. In all sites except Seattle, the proportions of positive tests for RSV and influenza in the 2020 community mitigation period were lower than predicted.

Conclusions: Between March and April 2020, rapid declines in ARI cases and the proportions of RSV and influenza in children were consistently noted across 7 US cities, which could be attributable to community mitigation measures against severe acute respiratory syndrome coronavirus 2."

Pediatrics: Longitudinal Outcomes for Multisystem Inflammatory Syndrome in Children (02 August 2021)

> "Background: In spring 2020, a novel hyperinflammatory process associated with severe acute respiratory syndrome coronavirus 2 multisystem inflammatory syndrome in children (MIS-C) was described. The long-term impact remains unknown. We report longitudinal outcomes from a New York interdisciplinary follow-up program.
>
> Methods: All children <21 years of age, admitted to NewYork-Presbyterian with MIS-C in 2020, were included. Children were followed at 1 to 4 weeks, 1 to 4 months, and 4 to 9 months postdischarge.
>
> Results: In total, 45 children were admitted with MIS-C. The median time to last follow-up was 5.8 months (interquartile range 1.3-6.7). Of those admitted, 76% required intensive care and 64% required vasopressors and/or inotropes. On admission, patients exhibited significant nonspecific inflammation, generalized lymphopenia, and thrombocytopenia. Soluble interleukin (IL) IL-2R, IL-6, IL-10, IL-17, IL-18, and C-X-C Motif Chemokine Ligand 9 were elevated. A total of 80% (n = 36) had at least mild and 44% (n = 20) had moderate-severe echocardiographic abnormalities including coronary abnormalities (9% had a z score of 2-2.5; 7% had a z score > 2.5). Whereas most inflammatory markers normalized by 1 to 4 weeks, 32% (n = 11 of 34) exhibited persistent lymphocytosis, with increased double-negative T cells in 96% of assessed patients (n = 23 of 24). By 1 to 4 weeks, only 18% (n = 7 of 39) had mild echocardiographic findings; all had normal coronaries. At 1 to 4 months, the proportion of double-negative T cells remained elevated in 92% (median 9%). At 4 to 9 months, only 1 child had persistent mild dysfunction. One had mild mitral and/or tricuspid regurgitation.
>
> Conclusions: Although the majority of children with MIS-C present critically ill, most inflammatory and cardiac manifestations in our cohort resolved rapidly."

Cardiovascular

Cardiol Young: Intriguing New Faces Of Covid-19: Persisting Clinical Symptoms And Cardiac Effects in Children (19 August 2021)

> "Objective: This study was conducted to evaluate the persisting Covid-19-related symptoms of the cases included in our study and to assess their cardiac findings in order to determine the impact of Covid-19 on children's cardiovascular health.
>
> Methods: In this study, 121 children between the ages of 0-18 with Covid-19 were evaluated based on their history, blood pressure values, and electrocardiography and echocardiography results. These findings were compared with the findings of the control group which consisted of 95 healthy cases who were in the same age range as the study

group and did not have Covid-19. The results were evaluated using the statistics program, SPSS 21.

Results: There was no significant difference between the study group and the control group in terms of age, weight, and body mass index. The clinical symptoms (chest and back pain, dizziness, headache, palpitation, fatigue, shortness of breath, loss of balance, coughing) of 37.2% of the cases persisted at least 1 month after Covid-19 recovery. Statistically significant differences were found in systolic blood pressure, left ventricular ejection fraction, relative wall thickness, and tricuspid annular plane systolic excursion.

Conclusion: The continuation of some cases' clinical symptoms post-recovery indicates that long Covid infection can be observed in children. The fact that statistically significant differences were observed between the echocardiographic parameters of the study and control groups suggests that Covid-19 may have effects on the cardiovascular system. To shed light on the long Covid cases among children and the infection's cardiac impacts, it would be beneficial to conduct more comprehensive studies on this matter."

Pediatrics: COVID-19 Vaccination-Associated Myocarditis in Adolescents (13 August 2021)

"Objective: This study aimed to characterize the clinical presentation, short term prognosis, and myocardial tissue changes associated with acute myocarditis following COVID-19 vaccination in the pediatric population.

Methods: In this retrospective multi-center study across 16 US hospitals, patients <21 years of age with a diagnosis of myocarditis following COVID-19 vaccination were included and compared to a cohort with multisystem inflammatory syndrome in children (MIS-C). Younger children with vaccine associated myocarditis were compared to older adolescents.

Results: 63 patients with a mean age of 15.6 years were included. 92% were male. All had received an mRNA vaccine and, except for one, presented following the 2nd dose. Four patients had significant dysrhythmia. 14% had mild left ventricular dysfunction on echocardiography which resolved on discharge. 88% met the diagnostic cardiac magnetic resonance (CMR) Lake Louise criteria for myocarditis. Myocardial injury was more prevalent in comparison to MIS-C patients. None of the patients required inotropic, mechanical, or circulatory support. There were no deaths. Follow up data obtained in 86% of patients, at a mean of 35 days showed resolution of symptoms, arrhythmias, and ventricular dysfunction.

Conclusions: Clinical characteristics and early outcomes are similar between the different pediatric age groups. There is evidence of myocardial inflammation and injury following mRNA COVID-19 vaccination as seen on CMR. The hospital course is mild with quick clinical recovery and excellent short-term outcomes. Close follow up and further studies are needed to understand the long-term implications and mechanism of these myocardial tissue changes."

Pediatrics: Symptomatic Acute Myocarditis in 7 Adolescents After Pfizer-BioNTech COVID-19 Vaccination (13 August 2021)

> "Trials of coronavirus disease 2019 (COVID-19) vaccination included limited numbers of children, so they may not have detected rare but important adverse events in this population. We report 7 cases of acute myocarditis or myopericarditis in healthy male adolescents who presented with chest pain all within 4 days after the second dose of Pfizer-BioNTech COVID-19 vaccination. Five patients had fever around the time of presentation. Acute COVID-19 was ruled out in all 7 cases on the basis of negative severe acute respiratory syndrome coronavirus 2 real-time reverse transcription polymerase chain reaction test results of specimens obtained by using nasopharyngeal swabs. None of the patients met criteria for multisystem inflammatory syndrome in children. Six of the 7 patients had negative severe acute respiratory syndrome coronavirus 2 nucleocapsid antibody assay results, suggesting no previous infection. All patients had an elevated troponin. Cardiac MRI revealed late gadolinium enhancement characteristic of myocarditis. All 7 patients resolved their symptoms rapidly. Three patients were treated with nonsteroidal antiinflammatory drugs only, and 4 received intravenous immunoglobulin and corticosteroids. In this report, we provide a summary of each adolescent's clinical course and evaluation. No causal relationship between vaccine administration and myocarditis has been established. Continued monitoring and reporting to the US Food and Drug Administration Vaccine Adverse Event Reporting System is strongly recommended."

Healthcare Workers

News in Brief

Long read: "'It's soul-draining': Health workers deployed to Covid hot zones are overwhelmed by deaths among the unvaccinated" (STAT).

Journal Articles

JAMA Intern Med: Association of Vaccine Type and Prior SARS-CoV-2 Infection With Symptoms and Antibody Measurements Following Vaccination Among Health Care Workers (16 August 2021)

> Research letter: "This cohort study evaluates symptoms following vaccination and antibody measurements in hospital workers who received an mRNA SARS-CoV-2 vaccine and had prior SARS-CoV-2 infection….

> Nearly 100% of HWs in this study mounted a strong antibody response to the spike protein after dose 2 of the SARS-CoV-2 mRNA vaccine independent of vaccine-induced reactions. Clinically significant symptoms following dose 1 were associated with prior SARS-CoV-2 infection, confirming prior reports. Clinically significant symptoms following vaccination were more frequent following dose 2 and receipt of the Moderna vaccine."

Medical Education

JAMA Netw Open: Midcareer Medical School Research Faculty Perspectives on Vitality and Professionalism During the COVID-19 Pandemic (13 August 2021)

> "Question: How do midcareer medical school faculty perceive the impact of the COVID-19 pandemic on their lives and their work?
>
> Findings: In this qualitative study of 39 midcareer research faculty, dominant themes included finding increased meaningfulness of work; a sense of professionalism and moral responsibility; enhanced relationships with colleagues; reassertion of career choice; disrupted research; impact on clinical work; attention to health disparities, social justice, and advocacy; increased family responsibilities; psychological stress; and focus on leadership.
>
> Meaning: In this study of a diverse group of midcareer medical school faculty, the experience of working during the pandemic appeared to have had important positive impacts on physician investigators and PhD scientists, contributing to their vitality and professional dedication that were associated with intrinsic motivators."

Mental Health, Psychosocial Issues, and Wellness

News in Brief

"How to handle the infuriating 'here we go again' feeling as the delta variant rages" (WP).

Long Reads

"Pandemic unveils growing suicide crisis for communities of color" (KHN; includes audio option).

"A radical plan to treat Covid's mental health fallout – The NHS is trialling a new approach to tackling physical and mental health issues: ask what really matters" (Wired).

Need a Mental Break? Take a Virtual Road Trip

"From 1969 to 2008, the writer and photographer John Margolies traveled the highways and back roads of America, photographing thousands of the unique and typically whimsical roadside signs and attractions that dotted the landscape—from a four-story fish to a 'foam house of tomorrow' to a hotel shaped like a beagle and much more" (Atlantic In Focus photos with selected items; view the digital collection from the Library of Congress).

Journal Articles

MMWR: Mental Health and Substance Use Among Adults with Disabilities During the COVID-19 Pandemic — United States, February–March 2021 (27 August 2021)

> "What is already known about this topic? Adults with disabilities experience higher levels of mental health conditions and substance use than do adults without disabilities.
>
> What is added by this report? During February–March 2021, 64.1% of surveyed U.S. adults with disabilities reported adverse mental health symptoms or substance use; past-month substance use was higher than that among adults without disabilities (40.6% versus 24.5%, respectively). Among adults with a diagnosis of mental health or substance use conditions, adults with disabilities more frequently (43% versus 35%) reported pandemic-related difficulty accessing related care and medications.
>
> What are the implications for public health practice? During public health emergencies, including the COVID-19 pandemic, enhanced mental health and substance use screening among adults with disabilities and improved access to related health care services are critical."

JAMA Psychiatry: Prevalence and Trends in Suicidal Behavior Among US Military Veterans During the COVID-19 Pandemic (25 August 2021)

> "Question: What is the population-based burden of the COVID-19 pandemic on suicidal behavior among US military veterans?
>
> Finding: In this cohort study of 3078 US military veterans, rates of suicide ideation and suicide attempts did not significantly increase from prepandemic to peripandemic at the population level. However, a small proportion of veterans (2.6%) developed new-onset suicide ideation during the pandemic.
>
> Meaning: These results suggest that despite grim forecasts about the COVID-19 pandemic possibly creating a perfect storm for suicidal behavior, the prevalence of suicidality did not appear to increase among military veterans nearly 10 months into the pandemic."

Eur J Psychotraumatol: The association between COVID-19 related stressors and mental health in refugees living in Australia (18 August 2021)

> "Objective: To evaluate the prevalence of COVID-19 related stressors and their relationship to key mental health and functioning outcomes in a resettled refugee sample.
>
> Method: N = 656 refugees and asylum seekers living in Australia completed a survey in June 2020 to index their mental health (posttraumatic stress disorder (PTSD), depression, health anxiety and disability) and COVID-19 experiences. The relationship between COVID-19 stressors and mental health was examined using a series of hierarchical linear regression models while controlling for other key demographic factors.
>
> Results: Refugees' most prevalent stressors related to worries of being infected by COVID-19 or the risk COVID-19 posed to others, which predicted health anxiety and PTSD. Social-related difficulties predicted depression and disability symptoms. Accessing and trusting information from authorities were the least prevalent stressors and were not significantly associated with mental health outcomes; neither was accessing basic supplies and financial support. Fears relating to the future such as concerns about visa application processes predicted health anxiety and disability. Crucially, the strongest predictor of all mental health outcomes was COVID-19 serving as a reminder of difficult past events.
>
> Conclusions: Refugees may be uniquely affected by COVID-19 because the pandemic serves as a reminder of their past conflict and persecution trauma. It is critical that mental health strategies accommodate the specific needs of refugees during the COVID-19 pandemic."

PLOS One: Mental health among healthcare workers and other vulnerable groups during the COVID-19 pandemic and other coronavirus outbreaks: A rapid systematic review (04 August 2021)

> "Introduction: Although most countries and healthcare systems worldwide have been affected by the COVID-19 pandemic, some groups of the population may be more vulnerable to detrimental effects of the pandemic on mental health than others. The aim of this systematic review was to synthesise evidence currently available from systematic reviews on the impact of COVID-19 and other coronavirus outbreaks on mental health for groups of the population thought to be at increased risk of detrimental mental health impacts.
>
> Materials and methods: We conducted a systematic review of reviews on adults and children residing in a country affected by a coronavirus outbreak and belonging to a group considered to be at risk of experiencing mental health inequalities. Data were collected on symptoms or diagnoses of any mental health condition, quality of life, suicide or attempted suicide. The protocol for this systematic review was registered in the online PROSPERO

database prior to commencing the review (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=194264).

Results: We included 25 systematic reviews. Most reviews included primary studies of hospital workers from multiple countries. Reviews reported variable estimates for the burden of symptoms of mental health problems among acute healthcare workers, COVID-19 patients with physical comorbidities, and children and adolescents. No evaluations of interventions were identified. Risk- and protective factors, mostly for healthcare workers, showed the importance of personal factors, the work environment, and social networks for mental health.

Conclusions: This review of reviews based on primary studies conducted in the early months of the COVID-19 pandemic shows a lack of evidence on mental health interventions and mental health impacts on vulnerable groups in the population."

Disparities and Health Equity

News in Brief

The 17 August 2021 issue of *The Journal of the American Medical Association (JAMA)* is devoted to the special topic "Racial and Ethnic Disparities and Inequities in Medicine and Health Care"; you can see the full issue at: https://jamanetwork.com/journals/jama/issue/326/7

Journal Articles

MMWR: Disparities in Excess Mortality Associated with COVID-19 — United States, 2020 (20 August 2021)

"What is already known about this topic? Hispanic or Latino, non-Hispanic Black or African American (Black), and non-Hispanic American Indian or Alaska Native populations have been disproportionately affected by the COVID-19 pandemic.

What is added by this report? Excess mortality incidence rates were higher for persons aged ≥65 years, with notable racial/ethnic disparities across all age groups. In 2020, among Black and Hispanic persons aged ≥65 years, >1,000 excess deaths per 100,000 person-years occurred compared with the number of deaths expected to occur.

What are the implications for public health practice? These findings could help guide targeted public health messaging and mitigation efforts to reduce disparities in COVID-19–

associated mortality in the United States, by identifying the racial/ethnic and age groups with the highest excess mortality rates."

JAMA Health Forum: Evaluation of Vaccination Strategies to Compare Efficient and Equitable Vaccine Allocation by Race and Ethnicity Across Time (20 August 2021)

"Question: What is the association of different vaccine allocation strategies with COVID-19–related morbidity and mortality and their distribution by racial and ethnic groups across time?

Findings: In this decision analytical model, the use of risk-based, age-based, and US Centers for Disease Control and Prevention (CDC)–phased vaccine allocation strategies was simulated. Risk-based strategies were associated with the largest estimated reductions in nonelective hospitalizations, death, and household transmissions compared with the CDC- and age-based strategies, with a similar proportion of Hispanic and Black patients being vaccinated early in the process compared with the CDC strategy.

Meaning: The study findings suggest that risk-based vaccine prioritization strategies could have the greatest effectiveness on reducing COVID-19–related deaths and household transmissions while ensuring equitable vaccine distribution."

JAMA Oncol: Use of an Analytics and Electronic Health Record–Based Approach for Targeted COVID-19 Vaccine Outreach to Marginalized Populations (19 August 2021)

Research letter: "This quality improvement study uses an analytics-based approach to examine which patients could potentially benefit from targeted nonelectronic communication regarding COVID-19 vaccination….

Our targeted outreach efforts identified and connected with patients who do not regularly use electronic communication and whose community networks may have been disrupted by the social isolation of the COVID-19 pandemic. This novel intervention demonstrated the potential benefits of an analytics-based strategy to reach marginalized patients at high risk for exclusion from electronic outreach and may be built on for future outreach programs."

Risk, Transmission, and Exposure

News in Brief

"Even moderate COVID restrictions can slow the spread of the virus — if they're timely" (NPR; see also: medRxiv preprint).

Ventilation

"We studied how to reduce airborne COVID spread in hospitals. Here's what we learnt" (Conversation).

"DIY air filters for classrooms? Experts are enthusiastic — and a citizen scientist makes it easy" (WGBH; see also: website with instructions and details).

Testing

"NIH scientists develop faster COVID-19 test" (NIH).

"Free rapid at-home coronavirus tests could make pandemic life easier – they may not be perfect, but sometimes speed is more important" (WP).

Journal Articles

Science: Airborne transmission of respiratory viruses (27 August 2021)

> Extensive review of airborne /aerosolized transmission of respiratory viruses, including SARS-CoV-2, with multiple figures and images:
>
> "The COVID-19 pandemic has revealed critical knowledge gaps in our understanding of and a need to update the traditional view of transmission pathways for respiratory viruses. The long-standing definitions of droplet and airborne transmission do not account for the mechanisms by which virus-laden respiratory droplets and aerosols travel through the air and lead to infection. In this Review, we discuss current evidence regarding the transmission of respiratory viruses by aerosols—how they are generated, transported, and deposited, as well as the factors affecting the relative contributions of droplet-spray deposition versus aerosol inhalation as modes of transmission. Improved understanding of aerosol transmission brought about by studies of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection requires a reevaluation of the major transmission pathways for other respiratory viruses, which will allow better-informed controls to reduce airborne transmission."

Elife: Superspreaders drive the largest outbreaks of hospital onset COVID-19 infections (24 August 2021)

> "The COVID-19 pandemic, caused by the SARS-CoV-2 virus, presents a global public health challenge. Hospitals have been at the forefront of this battle, treating large numbers of sick patients over several waves of infection. Finding ways to manage the spread of the virus in hospitals is key to protecting vulnerable patients and workers, while keeping hospitals running, but to generate effective infection control, researchers must understand how SARS-CoV-2 spreads. A range of factors make studying the transmission of SARS-CoV-2 in

hospitals tricky. For instance, some people do not present any symptoms, and, amongst those who do, it can be difficult to determine whether they caught the virus in the hospital or somewhere else. However, comparing the genetic information of the SARS-CoV-2 virus from different people in a hospital could allow scientists to understand how it spreads. Samples of the genetic material of SARS-CoV-2 can be obtained by swabbing infected individuals. If the genetic sequences of two samples are very different, it is unlikely that the individuals who provided the samples transmitted the virus to one another. Illingworth, Hamilton et al. used this information, along with other data about how SARS-CoV-2 is transmitted, to develop an algorithm that can determine how the virus spreads from person to person in different hospital wards. To build their algorithm, Illingworth, Hamilton et al. collected SARS-CoV-2 genetic data from patients and staff in a hospital, and combined it with information about how SARS-CoV-2 spreads and how these people moved in the hospital. The algorithm showed that, for the most part, patients were infected by other patients (20 out of 22 cases), while staff were infected equally by patients and staff. By further probing these data, Illingworth, Hamilton et al. revealed that 80% of hospital-acquired infections were caused by a group of just 21% of individuals in the study, identifying a 'superspreader' pattern. These findings may help to inform SARS-CoV-2 infection control measures to reduce spread within hospitals, and could potentially be used to improve infection control in other contexts."

JAMA Intern Med: COVID-19 Transmission Dynamics Among Close Contacts of Index Patients With COVID-19: A Population-Based Cohort Study in Zhejiang Province, China (23 August 2021)

"Question: Is there an association between the timing of exposure to and severity of COVID-19 disease in close contacts of index patients with COVID-19?

Findings: In this cohort study of 730 index patients with a COVID-19 diagnosis and 8852 close contacts, transmission potential was greatest in the first 2 days before and 3 days after onset of symptoms in the index patient. When contacts received a diagnosis of COVID-19 infection, they were more likely to present asymptomatically if they had been exposed to an asymptomatic patient.

Meaning: These results suggest that the quantity of exposure to a patient with COVID-19 may be associated with clinical presentation among close contacts who develop COVID-19."

J Hosp Med: Objective Measures of Physical Distancing in the Hospital During the COVID-19 Pandemic (18 August 2021)

"During the COVID-19 pandemic, hospitals published physical-distancing guidance and created dedicated respiratory isolation units (RIUs) for patients with COVID-19. The degree to which such distancing occurred between clinicians and patients is unknown. In this study, heat sensors from an existing hospital hand-hygiene monitoring system objectively tracked room entries as a proxy for physical distancing in both RIUs and general medicine units

before and during the pandemic. The RIUs saw a 60.6% reduction in entries per room per day (from 85.7 to 33.8). General medicine units that cared for patients under investigation for COVID-19 and other patients experienced a 14.7% reduction in entries per room per day (from 76.9 to 65.1). While gradual extinction was observed in both units as COVID-19 cases declined, the RIUs had a higher degree of physical distancing. Although the optimal level of physical distancing is unknown, sustaining physical distancing in the hospital may require re-education and real-time monitoring."

Nat Commun: SARS-CoV-2 disease severity and transmission efficiency is increased for airborne compared to fomite exposure in Syrian hamsters (17 August 2021)

"Transmission of SARS-CoV-2 is driven by contact, fomite, and airborne transmission. The relative contribution of different transmission routes remains subject to debate. Here, we show Syrian hamsters are susceptible to SARS-CoV-2 infection through intranasal, aerosol and fomite exposure. Different routes of exposure present with distinct disease manifestations. Intranasal and aerosol inoculation causes severe respiratory pathology, higher virus loads and increased weight loss. In contrast, fomite exposure leads to milder disease manifestation characterized by an anti-inflammatory immune state and delayed shedding pattern. Whereas the overall magnitude of respiratory virus shedding is not linked to disease severity, the onset of shedding is. Early shedding is linked to an increase in disease severity. Airborne transmission is more efficient than fomite transmission and dependent on the direction of the airflow. Carefully characterized SARS-CoV-2 transmission models will be crucial to assess potential changes in transmission and pathogenic potential in the light of the ongoing SARS-CoV-2 evolution."

J Infect Dis: Determinants and dynamics of SARS-CoV-2 infection in a diverse population: 6-month evaluation of a prospective cohort study (13 August 2021)

"Background: We studied risk factors, antibody responses, and symptoms of SARS-CoV-2 infection in a diverse, ambulatory population.

Methods: A prospective cohort (n=831, including 548 hospital-based healthcare workers) previously undiagnosed with SARS-CoV-2 infection was followed for six months with serial testing (SARS-CoV-2 PCR, specific IgG) and surveys.

Results: 93 participants (11.2%) tested SARS-CoV-2-positive; 14 (15.1%) were asymptomatic and 24 (25.8%), severely symptomatic. Healthcare workers were more likely to become infected (14.2% vs. 5.3%, aOR 2.1, 95% CI 1.4-3.3) and have severe symptoms (29.5% vs. 6.7%). IgG antibodies were detected after 79% of asymptomatic infections, 89% with mild-moderate symptoms, and 96% with severe symptoms. IgG trajectories after asymptomatic infection (slow increases) differed from symptomatic infections (early peaks within 2 months). Most participants (92%) had persistent IgG responses (median 171 days). In multivariable models, IgG titers were positively associated with symptom severity, certain

comorbidities, and hospital work. Dyspnea, altered smell and taste, and other neurologic changes persisted for ≥120 days in ≥10% of affected participants. Participants with prolonged symptoms (generally more severely symptomatic) had higher antibody levels.

Conclusions: In a prospective, ethnically diverse cohort, symptom severity correlated with the magnitude and trajectory of IgG production. Symptoms frequently persisted for many months after infection."

Health Messaging and Misinformation

News in Brief

"To boost Covid-19 vaccine uptake, one health system hunts for patients who fell through the cracks" (STAT).

"'Tainted' blood: covid skeptics request blood transfusions from unvaccinated donors" (KHN).

"As the coronavirus surges in Florida, some vaccine skeptics change their minds" (NPR).

Stanford Internet Observatory launches a new open-access journal (*Journal of Online Trust and Safety*) to cover research on online harm (Stanford).

Misinformation

"Louisiana doctors fight surge in COVID patients and misinformation over vaccines: 'We have two pandemics'" (CBS).

"The vaccine scientist spreading vaccine misinformation – Robert Malone claims to have invented mRNA technology. Why is he trying so hard to undermine its use?" (Atlantic).

"Facebook says post that cast doubt on covid-19 vaccine was most popular on the platform from January through March – The social-media platform's Saturday evening acknowledgment comes after a lengthy internal debate over whether to share data" (WP).

Long Reads

"A group of moms on Facebook built an island of good-faith vaccine debate in a sea of misinformation – As social media giants struggle to crack down on false claims about covid, ordinary users are finding ways to reach vaccine skeptics — and win them over" (WP; includes audio option).

Special Reports and Other Resources

NACCHO: Increasing Vaccine Confidence: A Resource Guide for Local Health Departments (17 August 2021)

"One important element of National Immunization Awareness Month (NIAM) is promoting vaccine confidence. Vaccine confidence is defined as the trust that patients, their families, and providers have in recommended vaccines; providers who administer vaccines; and the processes and policies that lead to vaccine development, licensure or authorization, manufacturing, and recommendations for use (CDC).

CDC has developed two toolkits for NIAM: Toolkit for Reaching Healthcare Professionals and Toolkit for Reaching Parents and Patients. These provide key messaging and information on maintaining routine immunizations and on COVID-19 vaccines that LHDs can use to educate on the importance of immunizations.

In addition to the CDC toolkits, NACCHO has developed Increasing Vaccine Confidence: A Resource Guide for Local Health Departments (LHDs). This guide was developed to provide tools and resources that LHDs can utilize to address vaccine confidence at the local level and among various populations. The resources included have been developed by federal, national, and local organizations and include toolkits, videos, fact sheets, model practices, and more.

We hope this guide provides useful tools LHDs can use to increase confidence in vaccines throughout their communities, both during NIAM and as we continue to get back on track with routine vaccines."

See also: National Immunization Awareness Month - Get Back on Track with Routine Immunizations

WHO: Tackling COVID-19 misinformation (social media toolkit) (04 August 2021)

"Ensuring communities have access to lifesaving public health information from trusted sources and are not misled by misinformation is essential to ending the COVID-19 pandemic.

In an effort to empower doctors and nurses – some of the most effective and trusted messengers of public health information – to actively address COVID-19 misinformation and build vaccine confidence globally, the WHO welcomes this social media toolkit for healthcare practitioners, developed by the Government of the United Kingdom.

This toolkit aims to provide healthcare workers with the tools, skills and content needed to effectively share authentic and reliable information online. Centered around three core

vaccine confidence messages, Vaccine Safety, Vaccine Development and Vaccine Reducing Risk of Sickness; this toolkit sets out three approaches: creating your own posts, posting the images and videos provided in the toolkit, or resharing vaccine information from trusted sources.

This product contributes to WHO's ongoing collaboration with the Government of the United Kingdom to raise awareness on and stop the spread of misinformation globally."

Journal Articles

Nat Med: Effects of a large-scale social media advertising campaign on holiday travel and COVID-19 infections: a cluster randomized controlled trial (19 August 2021)

"During the Coronavirus Disease 2019 (COVID-19) epidemic, many health professionals used social media to promote preventative health behaviors. We conducted a randomized controlled trial of the effect of a Facebook advertising campaign consisting of short videos recorded by doctors and nurses to encourage users to stay at home for the Thanksgiving and Christmas holidays (NCT04644328 and AEARCTR-0006821).

We randomly assigned counties to high intensity (n = 410 (386) at Thanksgiving (Christmas)) or low intensity (n = 410 (381)). The intervention was delivered to a large fraction of Facebook subscribers in 75% and 25% of randomly assigned zip codes in high- and low-intensity counties, respectively. In total, 6,998 (6,716) zip codes were included, and 11,954,109 (23,302,290) users were reached at Thanksgiving (Christmas).

The first two primary outcomes were holiday travel and fraction leaving home, both measured using mobile phone location data of Facebook users. Average distance traveled in high-intensity counties decreased by −0.993 percentage points (95% confidence interval (CI): −1.616, −0.371; P = 0.002) for the 3 days before each holiday compared to low-intensity counties. The fraction of people who left home on the holiday was not significantly affected (adjusted difference: 0.030; 95% CI: −0.361, 0.420; P = 0.881). The third primary outcome was COVID-19 infections recorded at the zip code level in the 2-week period starting 5 days after the holiday. Infections declined by 3.5% (adjusted 95% CI: −6.2%, −0.7%; P = 0.013) in intervention compared to control zip codes.

Social media messages recorded by health professionals before the winter holidays in the United States led to a significant reduction in holiday travel and subsequent COVID-19 infections."

JMIR Infodemiol: Examining the Public's Most Frequently Asked Questions Regarding COVID-19 Vaccines Using Search Engine Analytics in the United States: Observational Study (04 August 2021)

"Background: The emergency authorization of COVID-19 vaccines has offered the first means of long-term protection against COVID-19–related illness since the pandemic began. It is important for health care professionals to understand commonly held COVID-19 vaccine concerns and to be equipped with quality information that can be used to assist in medical decision-making.

Objective: Using Google's RankBrain machine learning algorithm, we sought to characterize the content of the most frequently asked questions (FAQs) about COVID-19 vaccines evidenced by internet searches. Secondarily, we sought to examine the information transparency and quality of sources used by Google to answer FAQs on COVID-19 vaccines.

Methods: We searched COVID-19 vaccine terms on Google and used the "People also ask" box to obtain FAQs generated by Google's machine learning algorithms. FAQs are assigned an "answer" source by Google. We extracted FAQs and answer sources related to COVID-19 vaccines. We used the Rothwell Classification of Questions to categorize questions on the basis of content. We classified answer sources as either academic, commercial, government, media outlet, or medical practice. We used the Journal of the American Medical Association's (JAMA's) benchmark criteria to assess information transparency and Brief DISCERN to assess information quality for answer sources. FAQ and answer source type frequencies were calculated. Chi-square tests were used to determine associations between information transparency by source type. One-way analysis of variance was used to assess differences in mean Brief DISCERN scores by source type.

Results: Our search yielded 28 unique FAQs about COVID-19 vaccines. Most COVID-19 vaccine–related FAQs were seeking factual information (22/28, 78.6%), specifically about safety and efficacy (9/22, 40.9%). The most common source type was media outlets (12/28, 42.9%), followed by government sources (11/28, 39.3%). Nineteen sources met 3 or more JAMA benchmark criteria with government sources as the majority (10/19, 52.6%). JAMA benchmark criteria performance did not significantly differ among source types ($\chi 24=7.40$; P=.12). One-way analysis of variance revealed a significant difference in mean Brief DISCERN scores by source type ($F4,23=10.27$; P<.001).

Conclusions: The most frequently asked COVID-19 vaccine–related questions pertained to vaccine safety and efficacy. We found that government sources provided the most transparent and highest-quality web-based COVID-19 vaccine–related information. Recognizing common questions and concerns about COVID-19 vaccines may assist in improving vaccination efforts."

Other Infectious Diseases

News in Brief

The FDA has approved TICOVAC, a vaccine to prevent tick-borne encephalitis (Pfizer).

"WHO forms new advisory group on origins of novel pathogens" (HPN).

"The newest disease detection tool for covid and beyond: poop" (KHN).

"USDA announces proposed framework for advancing surveillance for SARS-CoV-2 and other emerging zoonotic diseases through the American Rescue Plan" (USDA).

Outbreaks and Weird Cases

"Afghanistan almost beat polio. Now the future is uncertain" (Wired).

"Texas officials report 'unusual' anthrax case in a Hardeman County cow" (ONT).

Two human infections with a novel influenza A virus have been confirmed in Wisconsin (PV).

"7-year-old dies from rare brain-eating amoeba tied to California lake" (CBS).

"Cote d'Ivoire declares first Ebola outbreak in more than 25 years" (WHO).

Upcoming Events

WHAT: BSL4ZNet International Conference: Preparing and responding to new post-pandemic challenges

WHEN: 23 September – 14 October 2021 (virtual)

DETAILS: "The Biosafety Level 4 Zoonotic Laboratory Network (BSL4ZNet) is organizing a series of virtual sessions from September 23 to October 14, 2021. The sessions will feature keynote speakers, expert panelists and a moderated dialogue with questions and answers.

The 2021 BSL4ZNet International Conference will be organized into 4 thematic sessions focused on the post-pandemic era and driving science forward.

1. Emerging and re-emerging pathogens
2. BSL3 and BSL4 biosafety and biosecurity: international perspectives
3. One Health Perspectives
4. Zoonotic outbreaks and pandemics: science policy and science diplomacy perspectives"

REGISTER: https://pheedloop.com/register/bsl4znet2021/attendee/

Special Reports and Other Resources

WHO: Safety in administering medicines for neglected tropical diseases (13 August 2021)

> "The objective of this manual is to provide practical tools, including training modules and job aids, to help national programmes for neglected tropical diseases (NTDs) plan, prepareand monitor the safe administration of medicines for treatment of these diseases. The materials consolidate and emphasize critical aspects of existing guidance published by WHO; they do not make new recommendations.
>
> This manual summarizes key issues related to the safety of NTD medicines and their administration, with a focus on essential medicines used in mass drug administration (MDA), also called preventive chemotherapy. It can be used as a standalone reference manual, but is intended to be used in conjunction with the accompanying training modules, which provide practical instruction, and the aide-mémoires. Versions of the aide-mémoires and training modules are available respectively for both (i) programme managers and district-level health officials (Annex 1 and Web Annex A); and (ii) community drug distributors and community health workers (Annex 2 and Web Annex B)."

Journal Articles

Emerg Infect Dis: Resurgence of Respiratory Syncytial Virus Infections during COVID-19 Pandemic, Tokyo, Japan (13 August 2021)

> "More than a year into the coronavirus-19 pandemic, intensified infection control measures have controlled most viral respiratory infections in Tokyo, Japan. As of July 2021, however, an unusually high number of respiratory syncytial virus infections were reported in Tokyo. This resurgence may have resulted from restarting social activities for children."

JAMA Netw Open: Comparison of Antiviral Agents for Seasonal Influenza Outcomes in Healthy Adults and Children: A Systematic Review and Network Meta-analysis (13 August 2021)

> "Question: What antiviral agents for treating seasonal influenza are associated with the most safety and best outcomes among healthy adults and children?
>
> Findings: This network meta-analysis of 26 randomized clinical trials, including 11 897 patients, found that antiviral agents were associated with significantly greater efficacy than placebo in shortening the duration of influenza symptoms; zanamivir was associated with the shortest time to alleviation of influenza symptoms. Baloxavir was associated with a lower occurrence of influenza-related complications than other treatments.

Meaning: These findings suggest that zanamivir may be initiated as soon as possible for patients with influenza-like illness; in those who may be at high risk of developing influenza-related complications, baloxavir should be considered."

Microb Biotechnol: Clinical evidence that the pandemic from 1889 to 1891 commonly called the Russian flu might have been an earlier coronavirus pandemic (13 July 2021)

"Contemporary medical reports from Britain and Germany on patients suffering from a pandemic infection between 1889 and 1891, which was historically referred to as the Russian flu, share a number of characteristics with COVID-19. Most notable are aspects of multisystem affections comprising respiratory, gastrointestinal and neurological symptoms including loss of taste and smell perception; a protracted recovery resembling long covid and pathology observations of thrombosis in multiple organs, inflammation and rheumatic affections. As in COVID-19 and unlike in influenza, mortality was seen in elderly subjects while children were only weakly affected. Contemporary reports noted trans-species infection between pet animals or horses and humans, which would concur with a cross-infection by a broad host range bovine coronavirus dated by molecular clock arguments to an about 1890 cross-species infection event."

Statistics

	Total Cases	*Total Deaths*	*Total Vaccine Doses Administered*
Global	214,781,620	4,477,443	5,116,613,307
United States	38,387,116	633,591	364,694,303

JHU CSSE as of 1000 EDT 27 August 2021

Virginia	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	754,651	23,994	12,216	16,647	20,272	10,265	9,038	41,493
Hospitalizations	33,344	1,129	529	630	1,222	750	537	2,065
Deaths	11,769	319	186	246	282	209	198	432

VA DOH as of 1000 EDT 27 August 2021